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# TREATMENT OF ARTERIAL HYPERTENSION BY PENTA- AND HEXA-METHONIUM SALTS

## BASED ON 150 TESTS ON HYPERTENSIVES OF VARIED AETIOLOGY AND 53 PATIENTS TREATED FOR PERIODS OF TWO TO FOURTEEN MONTHS

BY

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Although from the therapeutic aspect it was the curarizing effects of the higher members of the methonium series which first attracted attention (Barlow and Ing, 1948a, 1948b ; Paton and Zaimis, 1948a), it soon became evident that the penta- and hexa-methonium halides, shown to be ganglion-blocking agents by Paton and Zaimis (1948b), were effective in producing reductions in blood pressure in normal and in hypertensive individuals (Arnold and Rosenheim, 1949 ; Arnold *et al.*, 1949 ; Paton and Zaimis, 1949 ; Burt and Graham, 1950 ; Hunter, 1950 ; and Davison, 1950). Preliminary tests carried out in this department (Restall and Smirk, 1950) indicated that good results could be obtained by the use of these substances as a mode of treatment in hypertension.

Further reports have been published on this use of penta- and hexa-methonium salts (Turner, 1950 ; Saville, 1950 ; Campbell and Robertson, 1950). No definite conclusions were reached by the first two authors, but Saville was hopeful that pentamethonium bromide would find a place in the treatment of hypertension. Both of these workers used relatively large doses to investigate effects, and neither reported the results of treatment over a long period. Campbell and Robertson (1950) report results similar to those of Restall and Smirk in respect of relief of such manifestations as headache and breathlessness. Further practical details concerning the management of cases are given by Smirk (1950a, 1950b, 1951), who claimed that effective blood-pressure reduction with subcutaneous injections of penta- or hexa-methonium bromide led to a clinical improvement in severe hypertensives which is of a higher order than that ordinarily obtained by other methods. The results obtained by oral therapy were much less reliable, though sometimes good. Turner (1951) has had similar results, and cites favourable experience in the toxaemic and other hypertensions of pregnancy. Frankel (1951) prefers hexa- to pentamethonium bromide, and regards intramuscular injection as more effective than oral dosage. Locket (1951), who has apparently used mainly oral therapy with hexamethonium bromide, regards the results as unsatisfactory. Bromism may occur. Locket thought there were patients who ceased to react to the substance.

The tests alluded to in this department convinced us of the possible usefulness of penta- and hexa-methonium salts in the long-term treatment of hypertensives, and accordingly we investigated the response to these methonium halides in 150 cases of hypertension of varied aetiology—benign essential (fixed, 72 ; labile, 15 ; following sympathectomy, 11) ; malignant (11) ; renal (nephritic, 7 ; surgical kidney, 3) ; pregnancy toxaemia (post-, 21 ; acute, 2) ; polycythaemia vera (1) ; and miscellaneous (7).

Fifty-three patients have been under treatment for periods of 2 to 14 months. Of these, 32 have been treated for six months or more. In selecting for treatment preference was given to those with the highest blood pressures, especially when the basal pressure was high, and to the patients with the most severe potentially reversible hypertensive manifestations. These included papilloedema, retinal haemorrhages, exudate, and oedema, cardiac asthma, hypertensive heart failure, cardiac enlargement and electrocardiographic changes, severe headache, dizzy and encephalopathic attacks, and minor strokes. Recently we have accepted patients over 65, but, at the outset, fear of cerebral and coronary complications decided us in most instances against treating patients in this age group.

Our main purpose has been threefold : (*a*) to investigate the effects of an adequate test dose which might give an indication of the possibility of treatment ; (*b*) to find if these methonium salts reduce blood pressure in hypertensives irrespective of aetiology ; and (*c*) to ascertain if hypertensive patients may be treated adequately with these methonium salts with relief of signs as well as symptoms. Our experience has indicated that, if postural effects were taken into account, a true index of potential reduction of blood pressure under treatment might be achieved by small subcutaneous test doses without adverse effects on the patient.

We record many instances of the relief of papilloedema, retinal oedema, and left ventricular failure, as well as of symptoms such as headache, dyspnoea, and vertigo. Turner (1950) seemed inclined to be diffident about symptomatic relief, and his experience with three cases urged him to caution in the use of these salts. Using smaller test doses, and being fully aware of the development of tolerance to the methonium salts, as well as utilizing postural effects in the treatment, we have experienced no complications in those patients we have treated, all of whom have shown symptomatic relief and objective improvement of one kind or another when signs were present.

It is not proposed to discuss the pharmacology of these methonium salts, so carefully worked out by various authors (Barlow and Ing, 1948a, 1948b; Paton and Zaimis, 1948a, 1948b, 1949; Balaban, Levy, and Wilde, 1949), and the pharmacodynamics of these salts in man is the subject of another paper in preparation (Restall and Smirk), but attention will be drawn to the development of tolerance which occurs in the course of treatment.

### Relation of Treatment to Pathogenesis

Many writers express the view that reduction of the blood pressure in arterial hypertension by sympathectomy or by drug action is a treatment of symptoms and a stopgap form of therapy to be employed only until some attempt can be made to correct the fundamental cause. In terms of other views on pathogenesis, the evidence for which is presented elsewhere (Smirk, 1949), the maintenance of the blood pressure as near to normal as practicable is much more than symptomatic treatment; on the contrary, effective blood-pressure reduction by suitable means is likely to arrest or retard pathological processes responsible for the development of the disorder.

According to this latter hypothesis there is no single or simple primary cause of essential hypertension. The disorder is thought to arise in some cases as the result of the simple overactivity of physiological processes, whereas in other cases pathological processes such as renal arteriolosclerosis may be primary. The fundamental concept is that, while initial blood-pressure increases may be, and commonly are, of composite origin, such pressure increases, if frequent, large, or prolonged, lead to a number of pathological and functional changes which tend further to maintain or elevate the blood pressure. Once this self-perpetuating cycle of changes has been set up the condition may be described as essential hypertension.

There is strong circumstantial evidence that many factors which raise the level of the blood pressure enhance strongly the liability to the subsequent development of essential hypertension. These include certain geographical environments, race, heredity, emotional lability or disposition to over-alertness and tenseness, occupation or domestic environment involving a tendency to stress and strain, over-average liability of the vasomotor system to respond by vasoconstriction to tenseness and emotion, physical activity or metabolic stimuli, over-average body weight or sthenic habitus. It is thought that such factors predispose to essential hypertension in so far as they are factors which tend of themselves to elevate somewhat the level of the blood pressure. When sufficient of these factors are present, or when they are present in a degree which may be regarded as pathological, the higher level of the blood pressure so engendered tends to set up pathological changes which of themselves perpetuate or increase further the initial blood-pressure rises.

The various pathological and functional changes induced as the result of primary blood-pressure rises (or excessive vasoconstriction), which, when they are developed, may lead to secondary blood-pressure rises, are thought to include such factors as the following: (*a*) inelasticity of large arteries; (*b*) exaggerated contraction of hypertrophied arterioles; (*c*) the release of pressor agents from ischaemic kidneys; (*d*) to a very minor degree, increased passive resistance of hypertrophied arterioles; and (*e*) an unknown non-renal factor or factors capable of perpetuating certain blood-pressure increases after the primary exciting causes of these increases have ceased to operate.

In terms of the above hypothesis the fundamental unity of the clinical picture in essential hypertension is not dependent upon the blood-pressure elevation being regarded as the result of a single or simple pathological process, it is due to the fact that the clinical manifestations and complications are caused almost entirely by events which are secondary to a single characteristic of the disorder—namely, high blood pressure—brought about mainly by vasoconstriction. It would follow that any condition associated with high blood pressure from any cause would be likely to lead, if the high pressure persisted for long enough, to the various pathological changes which, it is suggested, may be responsible for maintenance of existing increases or for further increases of the blood pressure in essential hypertension.

*Essential hypertension is both a syndrome and a disease. It is a syndrome in that its characteristic clinical and pathological features form part of all protracted high-blood-pressure cases, whatever the primary cause. It is a disease in that in the clinical entity we call essential hypertension the syndrome is the whole disorder. In nephritis, cortical hyperadrenalism, and many other conditions associated with blood-pressure elevation, the syndrome of essential hypertension is only part of the disease.*

*Evidence that our present knowledge of hypertension is consistent with the views expressed has been given elsewhere (Smirk, 1949). Holding provisionally such views, the authors prefer to regard effective blood-pressure reduction as a fundamental and not as a secondary objective in treatment. If it were found that effective reduction of the blood pressure would not retard the disorder, then the hypothesis would need revision. On the basis of this hypothesis the present paper is concerned with two matters: (1) can one obtain substantial control over the level of the blood pressure in various types of arterial hypertension, and (2) are there classes of patients in which blood-pressure reduction is beneficial?*

### Effects of Various Methods of Administration

We have administered penta- or hexa-methonium salts orally and by subcutaneous, intramuscular, and intravenous injection. Most of the results to be described here have been obtained with subcutaneous injection, and most of the formal tests have been made with hexamethonium bromide. In treatment, however, the effects of which have been closely observed, we have used almost as much penta- as hexa-methonium

bromide. In the course of treatment we have often gone from the one to the other without important subjective changes being apparent to the patient. A comparison of the hypotensive effects of penta- and hexa-methonium bromides is set out in Table III. It suggests that the hypotensive action of hexamethonium is usually the stronger. Patient 52, however, has always stated that pentamethonium has the stronger effect on her as judged by the occurrence of postural hypotension, and formal tests indicate that the pentamethonium has in her case a more powerful hypotensive action.

To prolong the effect we have tried intramuscular injection of a fine suspension in almond oil. Admixture with 1 in 400,000 to 1 in 100,000 adrenaline hydrochloride has been employed to slow absorption, and a number of investigations have been made with continuous subcutaneous injection over a 12-hour to 12-day period, using a device which empties the contents of a syringe (1–100 ml.) at a uniform rate over a selected period of time (2–32 hours). While the level of the blood pressure may be controlled in some cases by oral administration, the dose used is much larger even when it is administered with water before meals.

TABLE I.—*Comparison of the Effects of the Subcutaneous and Oral Administration of Hexamethonium Bromide*

| Case | Subcutaneous Administration | | | Oral Administration | | |
|---|---|---|---|---|---|---|
| | Dose (mg.) | Maximum B.P. Fall (Syst./Diast.) | Duration of Effect (Hours) | Dose (mg.) | Maximum B.P. Fall (Syst./Diast.) | Duration of Effect (Hours) |
| 40 | 160 | 80/26 | 6 | 1,500 | 96/52 | 9 |
| 127 | 170 | 66/36 | 5 | 2,250 | 50/30 | 5 |
| 59 | 100 | 60/22 | 4 | 1,500 | 100/35 | 6 |
| 49 | 225 | 62/58 | 4 | 1,500 | 25/6 | 5½ |
| 14 | 120 | 25/4 | 4 | 1,500 | 25/6 | 4½ |
| 126 | 75 | 50/28 | 2½ | 1,500 | 20/20 | 2 |
| 124 | 20 | 46/16 | 4½ | 1,250 | 40/32 | 9 |
| 50 | 110 | 88/47 | 4 | 2,500 | 60/10 | 5 |
| 135 | 30 | 30/7 | 3 | 500 | 20/12 | 5 |
| 131 | 15 | 40/15 | 3 | 500 | 15/4 | 3 |
| Average | 102·5 | 55/26 | 4 | 1,450 | 45/21 | 5½ |

*It should be emphasized that the larger doses set out in Table I, both oral and subcutaneous, are not to be administered until the patient has developed the requisite degree of tolerance to the action of the drug, otherwise there may be dangerous sequelae.* In the initial stages of our work it seemed preferable to avoid the uncertainties of alimentary absorption and to use the drug by an economical route so that more patients could be treated.

Subcutaneous administration has proved very satisfactory in that the levels of the blood pressures are largely predictable, the average duration of effect from a single injection being about three hours, though it has been longer, especially with larger doses. The disadvantage of subcutaneous injection is that with the smaller doses a maximal effect is ordinarily obtained within the first hour, and in some cases a dose large enough for effective lowering over a three-hour or four-hour period may cause giddiness when patients have been standing for a few minutes between the 15th and 60th minutes after injection.

In 30 patients doses of 15–25 mg. subcutaneously exercised their maximum hypotensive effect at the following times (in minutes) after the injection: 45, 36, 14, 27, 10, 40, 25, 30, 45, 30, 35, 50, 40, 45, 30, 25, 30, 40, 10, 45, 30, 45, 30, 20, 20, 30, 40, 20, 75, 35. When doses of 100–250 mg. are injected subcutaneously the maximum hypotensive effect often comes later, and in 16 patients the times (in minutes) were: 20, 55, 120, 120, 110, 60, 150, 55, 35, 150, 130, 75, 120, 17, 30, 25. The therapeutic regime should be adjusted to the individual response of the patient.

To overcome initial giddiness we gave intramuscular injections of a suspension in almond oil. These were effective in lessening the incidence of dizzy attacks on standing and they prolonged the action of the drug to eight hours. But it was felt that the preparation would be unsuitable for continual use. In a number of patients the addition of 1 in 100,000 adrenaline has prevented

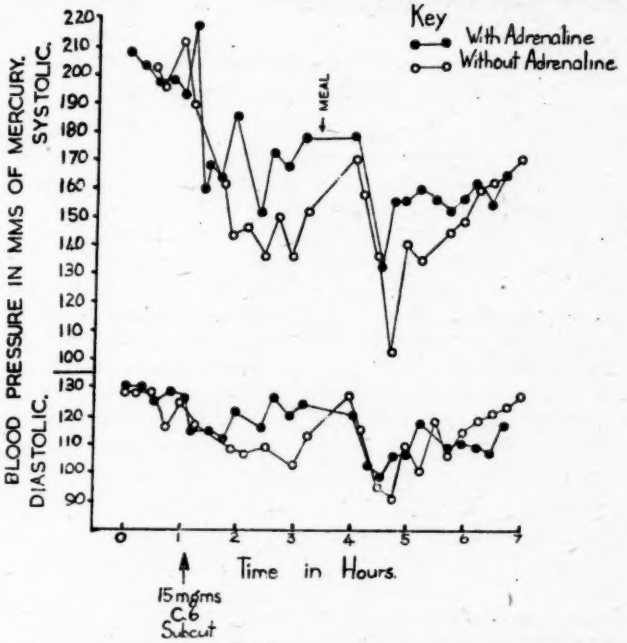


FIG. 1.—Effects of 15 mg. of hexamethonium bromide subcutaneously on the course of the blood pressure with and without the addition of 1/100,000 adrenaline hydrochloride. The additional fall of blood pressure after a meal is shown.

postural faintness shortly after administration without interfering much with the subsequent lowering of blood pressure.

When penta- or hexa-methonium salts are administered by means of an electrically operated syringe (Smirk, unpublished), it is possible to reduce the level of the blood pressure to a selected level and maintain this under quiet conditions with little alteration. Conversations with the patient involving emotional topics still raise the blood pressure considerably (Table II). Meals commonly cause a temporary

TABLE II.—*Effect of Emotion on the Blood Pressure in Patients While Under the Action of Hexamethonium Bromide*

| Case No. | Original Blood Pressure | Basal Blood Pressure | After Hexamethonium Bromide | Emotional Topic | Blood Pressure Rise |
|---|---|---|---|---|---|
| 29 | 272/150 | 224/140 | 162/114 | Physician enters; talks of illness | 28/22 |
| 40 | 240/140 | 234/136 | 157/105 | Visitors arrive | 27/25 |
| 41 | 240/120 | 160/80 | 158/108 | Business worries | 32/12 |
| | | | | Mental illness of mother | 42/22 |
| 49 | 258/141 | 196/106 | 176/104 | Disagreement with nursing staff | 28/18 |
| 54 | 220/160 | 172/110 | 118/86 | Her loss of memory | 24/12 |
| | | | | Separation from husband | 45/24 |
| 57 | 235/141 | 213/118 | 170/108 | Visitor arrives | 51/32 |
| 58 | 248/150 | 178/124 | 178/120 | Husband's war service, pilot in Battle of Britain | 62/20 |

rise followed by a more substantial pressure fall (Fig. 1). In some patients smoking raises the pressure. Many patients tolerate this automatic method of administration with few symptoms beyond dryness of the mouth, and the blood pressure may be maintained at the normal or near to normal level, day and night, for sessions of 12 days or more. There must be especial care during the hours of sleep, when the blood pressure will fall further. In anticipation of this the rate of injection of the drug should be reduced at about 5 p.m. There is a somewhat greater tendency to digestive upsets with this method of administration, perhaps because of the larger doses employed.

### Influence of Posture on Falls of Blood Pressure Induced by Penta- and Hexa-methonium Salts

A large majority of patients show blood-pressure falls after injection of penta- and hexa-methonium salts. Ordinarily the blood pressure falls progressively as the patient rises from the horizontal posture successively to semi-recumbency, sitting up in bed, sitting with the legs dangling, and finally to standing upright. This is of some importance from the point of view of initial investigation and treatment of patients, for if a large dose be administered to a patient recumbent a fall of blood pressure may be obtained, but should he sit or stand up at this time the dose may be sufficient to lower the pressure still further and syncope may occur. For example, some patients after injection of these methonium salts may exhibit falls of only 15 or 20 mm. of mercury in the systolic pressure when in the horizontal posture, but the systolic pressure may on occasion fall by 100 mm. of mercury when the vertical posture is assumed (Fig. 2 and Tables III, IV, and V).

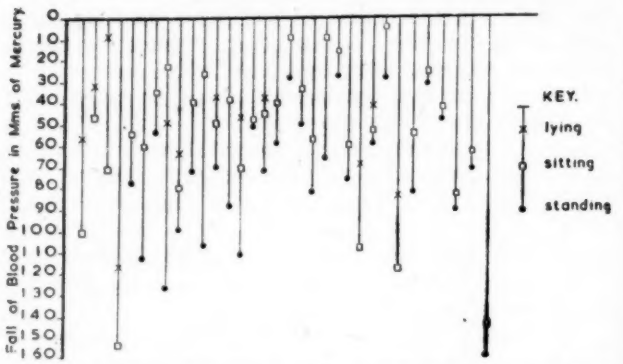


FIG. 2.—Effect of posture on the systolic blood-pressure level in 33 hypertensive patients following initial doses of 15 to 20 mg. of hexamethonium bromide subcutaneously. When patients are maintained in the horizontal posture the falls are rather less than those shown here. The diastolic-pressure falls are about one-third of the systolic falls.

We would point out that the knowledge of this occurrence prompted us to test patients in the sitting posture initially, for if the dose (15 mg.) produced a large fall (in some cases 150 mm. systolic and 90 mm. diastolic) the resulting low pressure might be accompanied by signs of faintness, which could quickly be remedied by placing the patient in a horizontal position. Indeed, by controlling posture we have been able to control the blood-pressure level as

TABLE III.—*Comparison of the Hypotensive Effects of Penta- and Hexa-methonium Bromides*

| Case No. | | Effect of Pentamethonium | | | | | | Effect of Hexamethonium | | | | | | Doses |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Standing | | Sitting | | Lying | | Standing | | Sitting | | Lying | | |
| | | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | |
| 52 | Before | 280/160 | 76 | 290/170 | 72 | 290/168 | 68 | 280/140 | 76 | 294/140 | 76 | 300/142 | 80 | 190 mg. C5 |
| | After | 140/98 | 76 | 204/120 | 72 | 220/122 | 68 | 160/100 | 80 | 214/126 | 72 | 270/142 | 76 | 190 mg. C6 |
| 58 | Before | 160/100 | 80 | 164/100 | 72 | 184/108 | 64 | 160/98 | 80 | 164/100 | 72 | 168/102 | 60 | 75 mg. C5 |
| | After | 108/68 | 100 | 124/88 | 84 | 150/100 | 72 | 84/58 | 88 | 112/78 | 88 | 145/90 | 72 | 75 mg. C6 |
| 59 | Before | 190/120 | 88 | 200/128 | 80 | 208/128 | 68 | 194/130 | 80 | 190/130 | 72 | 174/114 | 64 | 100 mg. C5 |
| | After | 112/80 | 120 | 134/98 | 112 | 170/110 | 92 | 104/78 | 124 | 138/94 | 100 | 190/124 | 80 | 100 mg. C6 |
| 133 | Before | 168/112 | 88 | 166/110 | 94 | 170/110 | 88 | 166/116 | 86 | 166/112 | 86 | 168/106 | 84 | 55 mg. C5 |
| | After | 102/80 | 98 | 122/88 | 90 | 138/74 | 78 | 50/? | 100 | 94/76 | 92 | 146/100 | 76 | 55 mg. C6 |
| 134 | Before | 166/132 | 86 | 164/130 | 82 | 168/126 | 78 | 168/132 | 82 | 178/132 | 84 | 168/122 | 88 | 35 mg. C5 |
| | After | 138/110 | 84 | 146/116 | 76 | 168/118 | 72 | 134/110 | 92 | 144/108 | 82 | 154/110 | 72 | 35 mg. C6 |
| 123 | Before | 188/104 | 72 | 200/110 | 68 | 190/102 | 64 | 190/104 | 64 | 200/110 | 64 | 220/120 | 60 | 120 mg. C5 |
| | After | 120/72 | 80 | 194/116 | 68 | 200/120 | 64 | 110/78 | 84 | 156/98 | 60 | 196/112 | 56 | 120 mg. C6 |

TABLE IV.—*Effect of Posture on the Blood Pressure and Pulse Rate Before and After Hexamethonium Bromide*

| Case No. | Before Hexamethonium | | | | | | After Hexamethonium | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Standing | | Sitting | | Lying | | Standing | | Sitting | | Lying | |
| | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. |
| 67 | 240/100 | 112 | 238/96 | 108 | 256/98 | 100 | 108/65 | 115 | 140/76 | 113 | | |
| 68 | 245/103 | 78 | 247/108 | 72 | 230/99 | 80 | 140/82 | 84 | 160/88 | 80 | 182/92 | 73 |
| 20 | 172/110 | 88 | 188/110 | 82 | | | 130/108 | 104 | 148/98 | 88 | 210/130 | |
| 135 | 160/90 | 100 | 174/102 | 96 | 168/98 | 96 | No reading | | 110/66 | 100 | 122/78 | 96 |
| 4 | 204/116 | 64 | 214/122 | 64 | 196/112 | 60 | 123/90 | 80 | 140/90 | 70 | 170/100 | 62 |
| 7 | 184/140 | 90 | 178/144 | 76 | 184/136 | 76 | 116/108 | 96 | 136/124 | 90 | 156/124 | 82 |
| 52 | 240/180 | 98 | 220/170 | 85 | 210/160 | 80 | 110/88 | 96 | 162/124 | 90 | 180/130 | 80 |
| 127 | 198/120 | 96 | 212/128 | 92 | 204/128 | 84 | 132/88 | 100 | 142/98 | 96 | 148/102 | 88 |
| 125 | 226/134 | 94 | 220/138 | 100 | 220/136 | 96 | 174/112 | 104 | 184/110 | 100 | 186/108 | 92 |
| 21 | 210/144 | 84 | 204/139 | 76 | 200/136 | 74 | 102/82 | 88 | 122/90 | 88 | 146/110 | 76 |
| 54 | 168/102 | 100 | 176/104 | 96 | 178/108 | 84 | 104/76 | 92 | 140/96 | 90 | 155/104 | 84 |
| 115 | 196/110 | 78 | 200/118 | 78 | 194/104 | 72 | 144/106 | 80 | 162/112 | 62 | 178/106 | 70 |
| 59 | 190/128 | 80 | 210/140 | 76 | 200/130 | 64 | 148/120 | 124 | 170/128 | 104 | 180/130 | 80 |
| 126 | 160/110 | 76 | 160/106 | 72 | 170/102 | 76 | 92/66 | 96 | 130/92 | 92 | 148/98 | 76 |
| 124 | 182/116 | 118 | 188/128 | 90 | 200/122 | 80 | 144/102 | 112 | 176/122 | 84 | 192/122 | 78 |
| 61 | 220/152 | 88 | 230/147 | 80 | 230/140 | 80 | 136/100 | 132 | 180/128 | 92 | 200/134 | 92 |
| 18 | 198/136 | 65 | 208/140 | 72 | 205/140 | 68 | 164/124 | 84 | 184/120 | 80 | 198/130 | 68 |
| 14 | 168/99 | 66 | 165/104 | 60 | 155/100 | 62 | 137/97 | 91 | 143/93 | 80 | 147/95 | 74 |
| 11 | 190/128 | 116 | 182/122 | 118 | 184/130 | 92 | 144/114 | 118 | 148/108 | 114 | 154/120 | 100 |

Doses have ranged from 15 to 150 mg. according to the state of tolerance which had developed at the time.

TABLE V.—*Effect of Posture on the Blood Pressure and Pulse Rate Before and After Hexamethonium Bromide in Patients who have had a Sympathectomy*

| Case No. | Before Hexamethonium | | | | | | After Hexamethonium | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Standing | | Sitting | | Lying | | Standing | | Sitting | | Lying | |
| | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. | B.P. | P.R. |
| 31 | 138/96 | 90 | 160/100 | 82 | 170/100 | 64 | 96/78 | 110 | 126/92 | 82 | 132/88 | 66 |
| 32 | 218/130 | 80 | 220/130 | 80 | | | 124/92 | 128 | 150/102 | 108 | 170/110 | 100 |
| 33 | 226/150 | 100 | 230/150 | 110 | | | 130/114 | 108 | 160/130 | 100 | | |
| 34 | 250/144 | 74 | 252/154 | 72 | 250/144 | 74 | 146/102 | 124 | 180/122 | 96 | 210/128 | 72 |
| 26 | 170/124 | 75 | 158/124 | 84 | 170/124 | 75 | 102/72 | 138 | 134/108 | 90 | 150/120 | 72 |
| 28 | | | 206/134 | | | | 142/110 | 116 | 188/134 | 112 | 238/92 | 84 |
| 104 | 172/114 | 92 | 178/110 | 84 | | | 100/74 | 100 | 128/98 | 64 | | |
| 30 | 148/102 | 76 | 178/120 | 84 | 182/118 | 76 | 110/70 | 90 | 138/106 | 88 | 142/100 | 80 |
| 27 | 190/124 | 76 | 216/132 | 72 | 220/126 | 68 | 110/74 | 112 | 162/102 | 100 | 202/114 | 80 |
| 25 | 190/126 | 69 | 216/132 | 60 | 220/122 | 57 | 132/106 | 94 | 158/110 | 81 | 163/107 | 63 |

Doses have ranged from 15 to 150 mg. according to the state of tolerance which had developed at the time.

desired. In this connexion it is of practical importance to remember that most patients are ambulant, and it is in this way that dosage can be adjusted suitably so that blood pressures in the standing and sitting postures are sufficiently but not excessively reduced, thus allowing of out-patient control of treatment.

## Influence of Blood-pressure Level on the Magnitude of Falls Induced by Hexamethonium Bromide

The hypotensive effect of a 15-mg. dose of hexamethonium bromide administered in the sitting posture is compared in 20 patients with mild and in 25 with severe degrees of arterial hypertension (Table VI).

TABLE VI.—*Influence of Blood Pressure Level on the Magnitude of Falls Induced by 15 mg. of Hexamethonium Bromide With Corresponding Pulse Rate Changes*

| Case No. | Diagnosis | Basal Blood Pressure | Before Hexamethonium | | After Hexamethonium | |
|---|---|---|---|---|---|---|
| | | | Casual B.P. | Pulse Rate | Fall of B.P. | Change of Pulse Rate |
| 113 | E.H. | | 278/138 | 68 | 40/14 | −4 |
| 34 | E.H. | 198/134 | 255/150 | 72 | 51/16 | +32 |
| 115 | E.H. | 204/116 | 248/125 | 70 | 16/+7 | 0 |
| 68 | E.H. | 176/92 | 246/110 | 68 | 104/26 | +12 |
| 127 | E.H. | 210/148 | 240/160 | 100 | 70/40 | −20 |
| 49 | M.H. | 196/106 | 240/140 | 99 | 108/42 | +9 |
| 130 | E.H. | 208/112 | 238/116 | 92 | 50/14 | −8 |
| 67 | E.H. | | 238/96 | 108 | 136/28 | +16 |
| 56 | P.T. | 198/140 | 238/154 | 96 | 78/34 | −4 |
| 101 | E.H. | 162/118 | 234/118 | 64 | 52/6 | +8 |
| 55 | M.H. | | 235/175 | 90 | 55/45 | +20 |
| 100 | P.T. | 216/148 | 230/150 | 80 | 28/10 | +4 |
| 105 | E.H. | 156/128 | 228/134 | 72 | 64/16 | +8 |
| 112 | E.H. | 162/98 | 228/112 | 88 | 82/24 | +16 |
| 131 | E.H. | 206/108 | 224/110 | 72 | 36/8 | |
| 125 | E.H. | 188/124 | 222/134 | 88 | 42/14 | +16 |
| 110 | E.H. | | 218/120 | 88 | 56/10 | 0 |
| 57 | P.T. | 213/118 | 220/120 | 96 | 46/+4 | +20 |
| 72 | P.T. | 168/116 | 218/136 | 84 | 38/10 | +12 |
| 38 | E.H. | | 216/102 | 102 | 84/28 | −2 |
| 16 | E.H. | 214/124 | 215/112 | 84 | 117/40 | +28 |
| 121 | P.T. | 206/134 | 214/138 | 100 | 10/+4 | −22 |
| 58 | P.T. | 178/124 | 212/136 | | 12/0 | |
| 63 | E.H. | 210/119 | 210/106 | 76 | 30/16 | +4 |
| 112 | E.H. | 162/98 | 210/116 | 72 | 40/14 | +4 |
| 82 | E.H. | 140/92 | 180/110 | 102 | 30/0 | +2 |
| 92 | E.H. | 134/100 | 180/98 | 50 | 46/6 | +2 |
| 20 | E.H. | 149/98 | 178/120 | 80 | 50/30 | +4 |
| 11 | R.H. | | 178/132 | 114 | 38/20 | +6 |
| 90 | P.T. | | 178/112 | 84 | 28/12 | +6 |
| 1 | E.H. | 160/102 | 176/104 | | 74/28 | 0 |
| 95 | E.H. | | 176/130 | | 38/24 | |
| 86 | E.H. | 136/88 | 174/120 | | 24/14 | |
| 135 | E.H. | 172/100 | 172/102 | 96 | 64/40 | −16 |
| 89 | P.T. | 148/106 | 170/114 | 78 | 16/4 | +9 |
| 80 | E.H. | 142/88 | 170/104 | 66 | 18/8 | +10 |
| 75 | E.H. | 124/86 | 170/98 | 72 | 38/2 | +6 |
| 44 | R.H. | | 170/126 | 82 | 22/10 | +36 |
| 91 | E.H. | | 170/108 | 88 | 22/14 | 0 |
| 8 | E.H. | 118/78 | 164/100 | 78 | 76/34 | +8 |
| 81 | E.H. | 128/86 | 162/118 | 58 | 42/28 | +14 |
| 92 | E.H. | 134/100 | 162/110 | 93 | 26/6 | +9 |
| 93 | P.T. | 124/88 | 162/96 | 70 | 28/0 | +2 |
| 108 | P. | 130/102 | 162/114 | 86 | 20/10 | +12 |
| 84 | E.H. | 146/90 | 160/90 | 72 | 22/2 | |

E.H.=Essential hypertension. M.H.=Malignant hypertension. P.T.=Post-toxaemic hypertension. R.H.=Renal hypertension. P.=Polycythaemia.

The degree of blood-pressure lowering induced by 15 mg. of hexamethonium bromide seems, on an average, to be greater when the initial casual systolic blood pressure is high. This is by no means an invariable relationship, and the statement is the expression only of a general tendency. In general the blood-pressure fall is also greater in cases selected for a high basal systolic pressure as contrasted with those exhibiting a low basal systolic pressure. There is no pronounced relationship between the initial diastolic pressure and the extent of the fall in diastolic pressure after 15 mg. of hexamethonium bromide.

## Basal-blood-pressure Lowering by Penta- and Hexamethonium Salts

In the absence of drug action blood-pressure lowering takes place under conditions of physical, metabolic, and emotional rest, and the resulting level is called the basal pressure (Addis, 1922; Alam and Smirk, 1943; Smirk, 1944). Kilpatrick (1948) has shown that in health the basal pressure is a physiological constant and in hypertension it varies much less than does the casual pressure.

Administration of adequate doses of penta- or hexamethonium bromide leads to decrease in the blood pressure to well below the basal level even with the patient in the horizontal posture (Fig. 3). Much smaller doses cause falls of pressure to below the basal level if the patient is in the semi-recumbent or the sitting posture. Small initial doses of 15 mg. of hexamethonium bromide, given subcutaneously in the sitting posture, decreased the blood pressure below the basal level in 29 out of 57 patients. Some of these results are seen in Table VI. In all of 10 patients whose blood pressure falls had not been to as low a level as the basal, the administration in the sitting posture of a larger dose brought the blood pressure below the basal level without difficulty.

It would appear that in the standing and sitting postures, and probably in the lying posture, the reduction of the blood pressure to below the basal level can be effected in almost all patients provided an appropriate dose is given. As will be shown later, the magnitude of the dose required depends upon the degree to which a state of toleration has developed; it might be anything from 15 to 300 mg. It is evident from the above statements that the substances cause reduction in the basal as well as in the supplemental (that is, casual minus basal) pressure, and that the casual blood pressure may be reduced below the original basal.

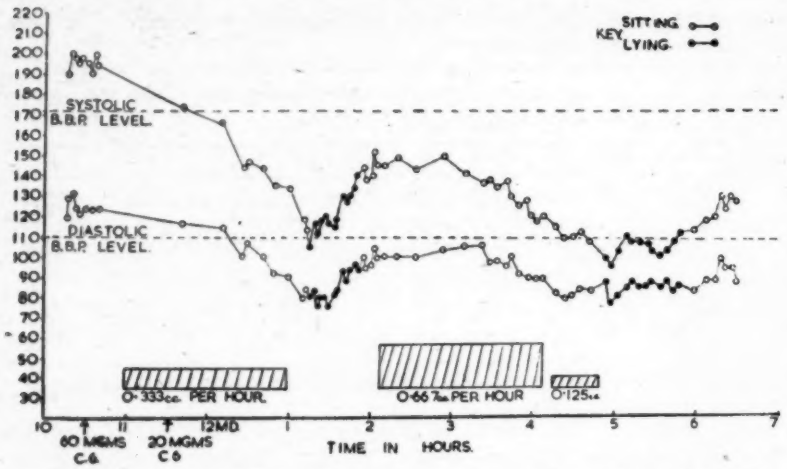


FIG. 3.—Effect of continuous subcutaneous injection of hexamethonium bromide on the blood pressure. Injection rates shown on the chart. In the sitting and lying postures the systolic and diastolic blood pressures are reduced to well below the level of the patient's basal blood pressure (B.B.P.).

### Effect of Penta- and Hexa-methonium Salts on the Pulse Rate

It has been remarked by Arnold and Rosenheim (1949) and Burt and Graham (1950) that the falls in blood pressure after administration of these methonium halides are accompanied by acceleration of the pulse. Certainly, sharp falls in blood pressure are usually associated with pulse acceleration, which may be as much as 20 or 30 beats a minute. Acceleration of the heart occurs with both penta- and hexa-methonium salts (Table III).

There is, however, no invariable relationship between the blood pressure and the pulse rate (Table VI). Blood-pressure falls are occasionally associated with slowing of the pulse. In some patients the fall of blood pressure ordinarily is accompanied by acceleration of the pulse, but if the blood-pressure fall is excessive, to low levels which cause faintness, then the pulse slows as it usually does in a fainting attack.

After months of treatment a proportion of patients exhibit less acceleration when the blood pressure falls, perhaps because of habituation to the lower blood-pressure level, possibly from improved heart action. In fact, cardiac acceleration and palpitation, which in some patients may be prominent in the early stages of investigation or treatment, are little cause for trouble later. For example, one patient's palpitation after hexamethonium bromide made us consider abandoning the treatment. The heart rate, however, was controlled by digitalis though no failure was present. After some months the digitalis was omitted and there was no recurrence of palpitation following the hexamethonium injections. In most patients palpitation has subsided without recourse to other drugs.

Ordinarily the change of pulse rate is more closely related to fall in blood pressure than to the amount of drug in the body; for example, there is often little change in the pulse rate when the patient remains in the horizontal posture, but when the patient assumes the vertical posture and the blood pressure falls the heart rate usually accelerates (Tables III and IV). This is evident in most hypertensives whether they have had a thoraco-lumbar sympathectomy or not. There is this difference: that, even though the pulse rates in these two groups have been comparable before a methonium salt was given, there is more pulse acceleration on standing in the sympathectomized hypertensive (Table V) than in the others.

### Response of Various Types of Arterial Hypertension to Hexamethonium Salts

Observations have been made on 150 patients with hypertension. Of these patients 88 have been investigated in a way which gives a rough idea of the magnitudes of the effects obtained injecting these methonium salts. Because factors such as the initial blood-pressure level influence the magnitude of the falls of blood pressure, the following figures should not be taken to indicate important differences in the responses of the different types of hypertension. All these tests were of three to four hours' duration, with blood-pressure measurements at intervals of about 10 minutes. They were carried out by trained technicians. Their presence throughout the tests has been an important factor in avoiding any reactions more unpleasant than transient faintness. The following results were obtained in the various groups of patients tested with a 15-mg. test dose of hexamethonium bromide given subcutaneously.

(*a*) Essential benign hypertension (46):
Average reduction, 48/19 mm.; Range 152/92—7/+4 mm.

(*b*) Malignant hypertension (7):
Average reduction, 39/24 mm.; Range 78/44—15/7 mm.

(*c*) Renal hypertension (11):
Average reduction, 31/12 mm.; Range 98/60—0/+14 mm.

(*d*) Toxaemic hypertension (14):
Average reduction, 37/13 mm.; Range 103/35—4/3 mm.

(*e*) Hypertensives with sympathectomy (10):
Average reduction, 61/25 mm.; Range 138/64—24/10 mm.

*Emphasis is placed on the fact that these results are from a small test dose (15 mg.) in the sitting position and that, with the exception of one or two nephritic patients, much greater falls in blood pressure were easily produced by larger doses of the drug.*

Our experience is that when a good fall is produced by a 15-mg. test dose given subcutaneously in the sitting posture there is seldom any difficulty in maintaining a reasonably low blood pressure in the course of treatment with suitable doses of methonium salts. In those cases where there is a poor response to the test dose of 15-mg. it is nearly always found that a larger dose produces a useful fall of blood pressure and that continued treatment is practicable.

It is not surprising that almost all cases show some fall in the level of the blood pressure irrespective of aetiology, because, even if the pressure rise in some instances is partly the result of a humoral mechanism, it would seem probable that those processes which normally maintain the tone of blood vessels still continue to operate. If this be so, decrease of nerve impulses by the blocking of sympathetic ganglia will still lead to a fall in the blood pressure as the result of the removal of normal sympathetic tone, and this would still be expected to happen even though the

elevation of the blood pressure were the result of a humoral mechanism which, it might be supposed, could not be overcome by the action of ganglion-blocking drugs.

### Tolerance to Penta- and Hexa-methonium Salts following Repeated Administration

Repeated administration of penta- or hexa-methonium salts in 53 cases under treatment indicates that some tolerance is acquired within a few days and the dosage needed to produce a given effect continues to increase for some weeks. After a time, however, the dose required does not need further increase. When tolerance has been acquired to one of the drugs

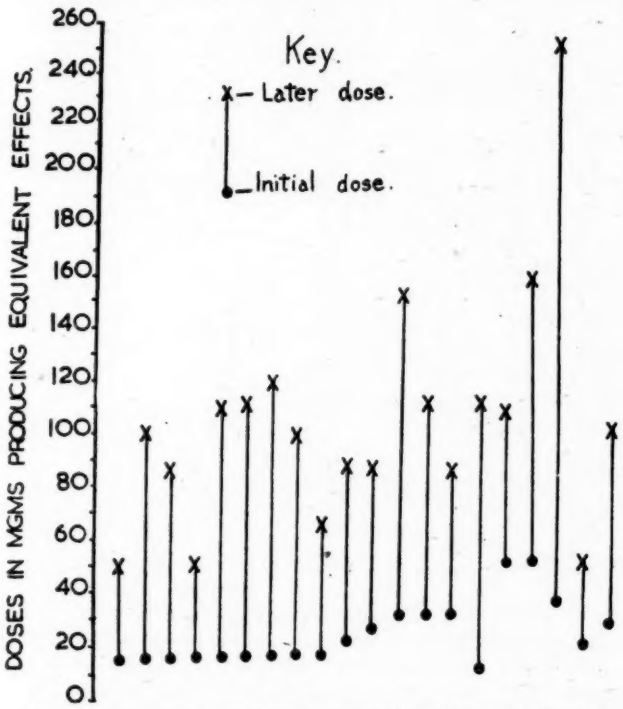


FIG. 4.—Comparison of the doses of hexamethonium bromide required to produce approximately equivalent effects before and after tolerance to the drug has been acquired as the result of repeated administration.

it is found that there is a corresponding increase of tolerance to the other. Fig. 4 indicates that five or ten times the original amount of drug may be required to produce the same effect after tolerance has developed. However, in a few instances, after several months of treatment, the dosage required to produce a given effect has actually diminished to slightly below the highest level.

### Improved Tolerance of Low Blood-pressure Levels following Repeated Administration of Penta- or Hexa-methonium Salts

There have been hypertensive patients who surprised us by showing no symptoms with blood-pressure falls of over 100 mm. Hg, even on the first clinical trial. Patients accustomed to blood-pressure levels of 220/130 or more have dropped to levels such as 110/80 and experienced no symptoms or only mild lightheadedness. Other hypertensives show symptoms before the pressure falls to classical normal levels such as 120/80. An occasional patient already feels faint at 170/105. More usually faintness first appears between 150 and 135 systolic. Most of our patients who have exhibited symptoms even when the pressure was above normal became habituated to lower pressures in the course of regular administration of penta- or hexa-methonium salts in doses large enough to bring the blood pressure down to just a little above the symptom level. This, of course, requires increase of the dose as tolerance develops. Table VII sets out the

TABLE VII.—*Improved Tolerance to Low Blood-pressure Levels Following Repeated Administration of Penta- or Hexa-methonium Salts*

| Case No. | Initial Blood Pressure | Symptoms Produced | Initial Blood-pressure Level at which Symptoms were Produced | Later Blood-pressure Level Tolerated Without Symptoms |
|---|---|---|---|---|
| 9 | 204/124 | Angina | 186/120 | 176/126 |
| 10 | 224/148 | Faintness | 72/56 | 120/90 |
| 14 | 248/136 | ,, | 104/78 | 104/78 |
| 16 | 266/155 | ,, | 128/96 | 100/76 |
| 17 | 210/130 | Dizziness | 180/145 | 118/85 |
| 29 | 242/140 | Faintness and vomiting | 138/90 | 104/76 |
| 30 | 178/120 | Lightheadedness | 110/70 | 112/98 |
| 52 | 226/152 | Faintness | 135/100 | 120/90 |
| 53 | 200/124 | ,, | 155/110 | 110/60 |
| 58 | 248/150 | Faintness and vomiting | 145/115 | 120/95 |
| 61 | 220/137 | Faintness | 164/130 | 148/102 |
| 13 | 204/158 | ,, | 110/70 | 128/88 |

blood-pressure levels which caused symptoms at the outset of treatment and contrasts them with the lower pressure levels which were well tolerated at a later stage of treatment. Hypertensives remain susceptible to the symptoms associated with lowered blood pressure, which, however, make their appearance at a lower level of the blood pressure than they did before the vascular system became habituated to a more normal level. The symptoms encountered are referred to in more detail later.

### Potentiation of Hexamethonium Salts by a Salt-poor Diet

At an early stage of this investigation one or two patients who had been taken off hexamethonium bromide because of a temporary shortage were placed on a Kempner salt-free diet. When supplies of the drug became available dosage at about the original level was resumed. One of our patients who had taken earlier doses without notable symptoms became unconscious, and another had an excessive fall of blood pressure to 95 systolic while lying flat and with the foot of the bed raised. This last patient experienced at rest a strong precordial pain which appeared to be anginal. Subsequent investigation showed that the Kempner diet and also a salt-poor diet without protein-deprivation (0.2 g. of sodium in 24 hours) enhanced the response to hexamethonium bromide.

Fig. 5 illustrates responses to 15 mg. of hexamethonium bromide before and during the administration of a salt-free diet. Observations on six other patients gave similar results and on one other an ambiguous result. There is therefore a definite indication that the blood-pressure-lowering effect of hexamethonium salts is enhanced by salt deprivation, an observation which is of clinical importance in the treatment of hypertensives, particularly those with congestive heart failure.

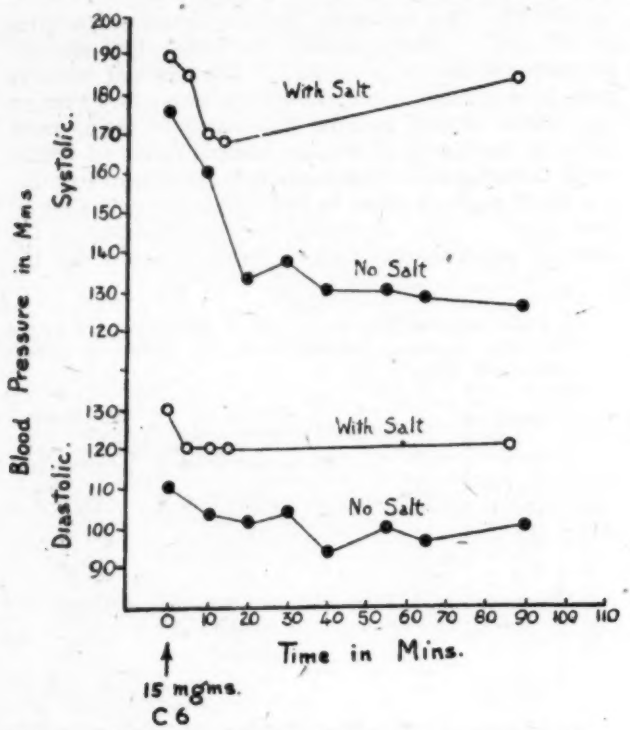


FIG. 5.—Effect of a salt-poor diet on the response to hexamethonium bromide.

### Effect of Penta- or Hexa-methonium Salts on Headache

One of the most striking symptomatic effects of the treatment of hypertension by penta- or hexamethonium salts is the relief of headache, which may be prompt and which may date from the inception of therapy. In 27 out of 29 consecutive cases with severe headache, relief was considerable or, more usually, substantially complete. By "substantially complete" it is meant that the headache was removed or if it remained it was considered by the patient to be infrequent and of inconsiderable magnitude. In most patients the headaches were relieved almost as soon as there was effective reduction of the blood-pressure level during the day and part of the night. In some patients the headaches were relieved only in the course of months. Avoidance of the horizontal posture during both day and night is an important factor in the relief of headache. In some instances sleeping in the sitting posture may by itself be sufficient to relieve a morning headache. *Recurrences of headache can nearly always be traced to a break in the therapeutic regime such as failure to raise the dose of hexamethonium bromide as tolerance develops.* Patients have also stated spontaneously that, in addition to relief of headaches, the head feels clearer and they themselves feel brighter in the morning. This statement has been volunteered so many times that it would appear that the lack of brightness and general feeling of sluggishness common in the morning in hypertensives is often relieved in this way. Table VIII sets out a summary of these results. The relief is not confined to any particular type of hypertension and is not dependent on rest in bed. A few observations have been made with other types of headache, as, for example, those due to migraine—so far without relief.

Although hypertensive headache is relieved by penta- or hexa-methonium injections, these may on occasion induce a headache, which, however, is ordinarily of a different character and less severe than the hypertensive headache. This occurs especially when the blood pressure falls precipitously, and sometimes may be avoided by adding 1 in 200,000 adrenaline hydrochloride to the drug, so as to lessen the rate of absorption.

TABLE VIII.—*Effect of Penta- and Hexa-methonium Salts on Headache*

| Case No. | Previous Duration of Headaches | Severity of Headaches | Duration of Treatment | Degree of Relief |
|---|---|---|---|---|
| 55 | Mainly 5-6 months. Some for 2 years | Severe | 6 months | Almost complete |
| 53 | 16 months | ,, | 10 ,, | Substantially complete |
| 51 | Several years | Troublesome | 11 ,, | ,, ,, |
| 47 | Occasional headaches for 12 months | Troublesome in morning | 11 ,, | Complete |
| 52 | Headaches for as long as she can remember | Very severe | 14 ,, | Substantially complete |
| 41 | 3 months | Mild | 7 ,, | Complete |
| 40 | Every night for several years | Severe | 8 ,, | Almost complete—about one per month |
| 17 | Morning headaches about 8 years | ,, | 8 ,, | Complete relief |
| 61 | 9 years—since 2nd pregnancy | ,, | 7 ,, | Much less |
| 60 | 2 years | Severe—sometimes lasting a week | 11 ,, | Considerable |
| 14 | Many years | Very severe | 14 ,, | Complete |
| 16 | Headache | Severe | 9 ,, | Considerable |
| 21 | Since discharge from Navy in 1946 | ,, | 8 ,, | Complete |
| 59 | 3 years | Moderate | 9 ,, | Substantially complete |
| 56 | 1 year | Severe | 6 ,, | Almost complete |
| 42 | 1 ,, | Moderate | 7 ,, | Complete |
| 49 | Dull headaches almost every a.m. for 4 years | ,, | 7 ,, | ,, |
| 57 | Increasing generalized headaches for last 2 or 3 years | Severe | 7 ,, | ,, |
| 76 | Headache | ,, | 6 ,, | ,, |
| 100 | 6 months | ,, | 4 ,, | Much improved |
| 105 | 8 years | | 3 ,, | Improved |
| 115 | 5 ,, | Very severe | 1 month | Substantially complete |
| 122 | 8 ,, | Severe | 2½ months | Almost complete |
| 123 | 1 year | Moderate | 5 weeks | Complete |
| 125 | Mornings for some time | Severe | 2 months | ,, |
| 142 | "Years" | Difficult to evaluate | 1 month | Little difference |
| 134 | 2 years | Mild occipital | 1 ,, | Complete |
| 107 | 1 year | Moderate | 1 ,, | Substantially complete |
| 136 | 1 ,, | Very severe | 1 ,, | Little difference |

### Effect of Penta- and Hexa-methonium Salts on the Incidence of Encephalopathy and Dizzy Attacks

Of the patients treated, six had experienced definite attacks of encephalopathy in the sense of having attacks either of unconsciousness or of paralytic phenomena with rapid recovery. The number of attacks of encephalopathy before treatment was comparatively few and there have been three recurrences of short duration since treatment started. It seems that encephalopathic attacks are not prevented. Spontaneous dizzy attacks, however, were frequent in seven patients, and were stated to be completely relieved by treatment. While this is purely subjective, there is a case for further study of the probability that treatment with these methonium halides may lessen the tendency to spontaneous dizzy attacks, and it is proposed to give further attention to the question of whether the incidence of encephalopathic attacks is influenced by them.

It should be borne in mind that most patients on adequate dosage of penta- or hexa-methonium salts experience slight or moderate faintness occasionally on

standing quietly. Intelligent patients distinguish spontaneous dizzy attacks from the faintness induced by hypotension. Until a specific inquiry is made into the character of the sensation, they tend to describe both sensations as "dizzy turns." The sensations induced by the drug are relieved promptly by the sitting or lying posture.

### Effect of Penta- and Hexa-methonium Salts on Hypertensive Changes in the Retinae

In this department stress has always been laid on the observation of the retinae in hypertension, and we have had the advantage of the opinion of Mr. Rowland Wilson in many instances. In this series our own observations were augmented by his and those of senior members of the Neurosurgical Department. When differences of opinion arose this will be indicated in the text. In all of 25 patients under treatment who had such reversible retinal changes as haemorrhages, soft exudates, or retinal oedema we observed distinctive improvement, and in many instances disappearance of the abnormality. This was particularly evident in the case of haemorrhages and of retinal oedema which was not located in the immediate vicinity of the disk, when complete disappearance could be anticipated. Soft exudate sometimes disappears, but we have not had many examples of soft exudates in this series.

Cases with papilloedema were sought out especially for treatment, and 12 were available for study and have been examined at frequent intervals. Eleven of these were examples of malignant hypertension. One patient, though papilloedema was present, appeared on other grounds to be an example of advanced essential hypertension. *It has been clear to all observers that in all patients with papilloedema treated for two months or more there has been either disappearance or a substantial diminution of the abnormality.* Ordinarily, improvement was evident in a month or less. It will be realized that, although there is no difficulty in detecting the presence of appreciable papilloedema or retinal oedema, it is often particularly difficult to decide whether these have entirely disappeared, leaving behind only those permanent changes which sometimes remain when papilloedema has disappeared—as, for example, a hazy edge to part of the disk and some loss of translucency of the disk and immediately surrounding structures.

It will be clear that the distinction between residual circumpapillary oedema and papilloedema, and the permanent changes which follow these, is not always a matter which can be decided with finality. Such differences of interpretation as have arisen have always been on this point. The opinion here expressed is, so far as we can make it, a conservative one compounded of our own and of the views of several observers who have been kind enough to help us. That there has been diminution in the extent of these retinal changes is agreed by all observers. All cases have improved to a stage where the presence of a physiological cup was generally accepted. In almost all cases one eye, and sometimes both eyes, improved to a stage where it was generally accepted that all papilloedema had disappeared from that eye. Not infrequently, however, the other eye, though exhibiting a physiological cup, would retain a fuzzy edge to a part or sometimes to the whole of the disk circumference.

In three instances, after several months, we observed return of papilloedema while the patient was still under treatment. In one case this occurred in hospital in the course of intercurrent pneumonia; it subsequently disappeared completely from both eyes, and several months later recurred to a slight extent in one eye at a time when the patient was making further clinical improvement subjectively. In another case it recurred in both eyes in an out-patient case during an attack of glandular fever; it disappeared completely in one eye and was greatly diminished in degree in the other eye coincidentally with intensified treatment. The third case, seen recently, exhibited a slight oedema of the disk edge without loss of the physiological cup at a time when treatment seemed effective in other respects. In three patients treated by continuous injection of hexamethonium bromide, securing day and night blood-pressure reductions of the order of 80–100 mm. systolic and 30–40 mm. diastolic, the papilloedema had disappeared from one eye in each patient within 12 days of treatment and had decreased to a considerable extent in the other eye.

### Effect of Penta- and Hexa-methonium Salts on Circulatory Manifestations in Arterial Hypertension

We have directed attention to the effect of penta- and hexa-methonium salts on breathlessness, gallop rhythm, alternation of the pulse, heart size, nose-bleeds, and the presence or absence of angina pectoris.

*Breathlessness* was complained of in varying degrees by 21 patients who were treated with penta- or hexa-methonium salts. There was an appreciable measure of improvement in all (Table IX). These patients, in addition to treatment with penta- or hexa-methonium salts, had the advantage of rest in hospital. Six of these patients were given a salt-poor diet in order to economize in the amount of drug employed. The degree of improvement even in these cases appeared to be considerably greater than we have ordinarily experienced on salt restriction without the use of these methonium halides. Of the 21 patients who originally had breathlessness 19 have been maintained on treatment and improvements have been sustained. Eighteen of these are now out-patients and 17 have climbed 32 or more steps without discomfort. At the present time only one of these patients is on digitalis and none are on mersalyl. One of the two remaining patients, whose breathlessness had improved, disliked injections and declined further treatment. The blood pressure rose again and she had a further cerebral haemorrhage about 14 days after injections ceased. The other of the two maintained a blood-pressure fall without injections, so these were terminated.

Two other patients with arterial hypertension and congestive heart failure, not included in the series of 21, received a few injections of hexamethonium bromide without either favourable or unfavourable response. Treatment was not continued in the one case because of a local haemorrhagic reaction to injections, and in the other because, apart from injections, the presence of polyfocal ventricular premature systoles, with occasional R waves interrupting the antecedent T waves, suggested the probability of added risk to life.

Improvement was particularly dramatic in two patients with malignant hypertension and cardiac asthma treated day and night by continuous blood-pressure reduction to approximately normal levels for periods of 12 days. In both cases rest had failed to

TABLE IX.—*Effect of Penta- and Hexa-methonium Salts on Breathlessness*

| Case No. | Case Age | Diagnosis | Before Treatment | During Treatment | Other Treatment |
|---|---|---|---|---|---|
| 55 | 44 | Malignant hypertension | Breathless getting out of bed | Walks slowly on flat without breathlessness | None |
| 51 | 58 | ,, ,, | Breathless in bed | Does very light jobs on farm; not breathless on flat. Slightly breathless on slopes | Mersalyl and salt-poor diet |
| 52 | 47 | ,, ,, | ,, ,, | Walks up 62 steps without difficulty | Salt-poor diet |
| 76 | 43 | ,, ,, | Repeated cardiac asthma. Breathless on walking a few steps | No nocturnal breathlessness. Walks up 31 steps without breathlessness | None |
| 49 | 52 | ,, ,, | Repeated cardiac asthma, almost every night for 1 month. Bed 2 years | ,, ,, ,, | ,, |
| 99 | 70 | Essential hypertension | Cardiac asthma. Breathless on slight exertion when up | No nocturnal breathlessness. Less breathless on exertion | Digitalis |
| 73 | 69 | ,, ,, | Cardiac asthma frequent. In bed 2 years | No nocturnal breathlessness. Now beginning to get up. Able to walk 200 yards on flat without breathlessness | None |
| 41 | 48 | ,, ,, | Breathless on stairs | Climbs stairs and hills slowly | ,, |
| 40 | 58 | ,, ,, | Breathless in bed | Walks up stairs holding conversation | Salt-poor diet |
| 13 | 54 | ,, ,, | Breathless on stairs and hill | Much less breathless; tested in same places | ,, ,, |
| 17 | 53 | ,, ,, | ,, ,, ,, | Tried same situations: definitely less breathless | None |
| 58 | 36 | Post-toxaemic hypertension | Slightly breathless only | No breathlessness in same circumstances | ,, |
| 14 | 48 | Essential hypertension | Breathless when gardening | Not breathless gardening | Salt-poor diet |
| 60 | 41 | Post-toxaemic hypertension | Breathless with housework | Definitely less breathless | ,, ,, |
| 59 | 42 | ,, ,, | Breathless on stairs | Not breathless on stairs | ,, ,, |
| 100 | 43 | ,, ,, | Moderately breathless at rest | Not breathless at rest or with moderate housework | None |
| 125 | 52 | Essential hypertension. Aortic regurgitation | Cardiac asthma severe. Very breathless on effort | Cardiac asthma mild. Still breathless on exertion | None, but will require digitalis |
| 127 | 56 | Essential hypertension | Congestive heart failure. Breathless at rest | Walks up 32 steps without discomfort | Digitalis. Improved without alteration of dose |
| 134 | 50 | ,, ,, | Cardiac asthma. Congestive heart failure. Breathless at rest | ,, ,, ,, | Failed while on moderate salt restriction—regime unaltered. No digitalis. No mersalyl |
| 133 | 50 | ,, ,, | ,, ,, ,, | Unrelieved by hexamethonium alone; relief on adding digitalis | Digitalis |
| 56 | 40 | Post-toxaemic hypertension | Congestive heart failure. Breathless at rest; gross leg oedema; basal rales | Improved, but recurred when off treatment. Improved when treatment restored. Now climbs 32 steps | None |

bring relief. No attack occurred after the starting of treatment. Both patients noted that, apart from lessened breathlessness, they could breathe more deeply. The vital capacity in one of the patients increased in the 12 days from 0.9 to 2.1 litres.

Other circulatory changes were not observed in a sufficient number of instances. Of five patients who had over two months' treatment a gallop rhythm disappeared in four and was barely audible in the other. However, we do not attach great prognostic importance to gallop rhythm in hypertension. Alternation of the pulse was noted before treatment in two patients and was absent after treatment.

*Nose-bleeds* were complained of by five patients. There has been very little nose-bleeding since treatment started.

*Angina* was present in seven patients. Attacks were induced by over-lowering of the blood pressure in two patients and with slight lowering in one patient. Four patients who received treatment for two months or more appeared to have fewer attacks. This result was unanticipated, and the relief of symptoms may well be coincidental, though theoretically it is possible that the lowering of the blood pressure reduced the work to be done by the heart to a degree which is out of proportion to the decrease in the coronary flow that results from a lower arterial pressure. If there are indeed cases which receive genuine benefit it seems probable that others will be made worse. In any case, the administration of methonium salts to anginal patients is a matter which we have regarded as an indication for extreme caution.

*Radiographic observations* were made on 15 patients treated with penta- or hexa-methonium salts over periods of 2 to 14 months. Reduction in the degree of pulmonary congestion was noted in all of the four patients in whom congestion was present at the inception of treatment. Certain changes in the frontal silhouette of the heart occurred; some of these were well within the limits of experimental error, the differences being so small that no conclusion could be drawn concerning change in the size of the individual patient's heart. Taking all the results together, however, there is an indication that slight reduction in the size of the heart is not unusual whether judged by the whole silhouette or the transverse diameter (Table X).

TABLE X.—*Change in the Transverse Diameter of the Heart During Treatment With Penta- or Hexa-methonium Bromides*

| Case No. | Initial Transverse Diameter (cm.) | Change in Transverse Diameter (cm.) | Time Interval (Weeks) |
|---|---|---|---|
| 52 | 17·0 | −3·0 | 56 |
| 127 | 15·8 | −1·7 | 9 |
| 134 | 20·4 | 0 | 2 |
| 47 | 13·4 | −0·8 | 11 |
| 55 | 14·6 | −0·2 | 9 |
| 13 | 14·2 | −0·9 | 40 |
| 14 | 12·5 | −0·5 | 36 |
| 41 | 15·3 | −0·4 | 13 |
| 54 | 14·1 | −0·4 | 16 |
| 57 | 16·0 | +0·5 | 6 |
| 51 | 14·3 | +1·2 | 38 |
| 53 | 14·1 | −0·5 | 34 |
| 76 | 17·0 | −2·1 | 46 |
| 63 | 13·7 | −0·4 | 9 |
| 49 | 17·4 | 0 | 12 |
| Average | 15·3 | −0·6 | 22·5 |

The algebraical average of the changes is a decrease of 0.61 cm. in transverse diameter. Eleven of the above-mentioned patients had shown impairment in exercise tolerance, and all of these were improved during methonium treatment.

*Electrocardiographic changes* due to arterial hypertension were present in eight of the cases in which our

observations extended over several months. In all instances changes were observed in the direction of return towards a more normal trace. In cases of moderate severity inverted T waves became positive; in severe cases the T wave inversions remained, but ST segment deviations decreased or disappeared. Such changes were most evident in the first limb lead and in the fifth and sixth (V) chest leads. Unipolar limb leads sometimes showed similar changes.

### Effect of Penta- and Hexa-methonium Salts on Renal Excretion in Hypertensive Patients with Impairment of Renal Function

Our observations here are confined to four patients whose high blood pressure was associated with renal insufficiency. In no case was effective blood-pressure reduction associated with rise in the non-protein nitrogen, or with symptomatic indication of impairment in the excretory functions of the kidneys. It is clear that any patient with impairment in the excretory functions of the kidneys requires careful study in regard to the effect of blood-pressure lowering before such treatment is adopted as potentially of therapeutic value. Such results as have been obtained indicate that there are at least some patients whose excretory capacity is not reduced when the blood pressure is lowered by methonium halides.

*Case 47.*—Male aged 27. Chronic nephritis. Urea concentration, 1.16%. When off hexamethonium bromide the casual blood pressure was in the region of 220/125 and the T.N.P.N. was 43 and 50 mg./100 ml. When under treatment the blood pressure was in the region of 148/90 and the T.N.P.N. was 42 mg./100 ml.

*Case 42.*—Male aged 40. Advanced renal tuberculosis. Urea concentration, 1.1%. When off hexamethonium bromide the casual blood pressure was in the region of 190/100 and the T.N.P.N. was 62, 93, 42, and 76 mg./100 ml. When under treatment with hexamethonium bromide the blood pressure was in the region of 135/87 and the T.N.P.N. was 78, 74, 62, 57, 58, 72, 64, and 75 mg./100 ml.

*Case 55.*—Female aged 45. Malignant hypertension. Urea concentration, 0.98%. When off treatment the casual blood pressure was in the region of 265/170 and the T.N.P.N. was 66 mg./100 ml. When under treatment with hexamethonium bromide the blood pressure was commonly in the region of 180/110 and the T.N.P.N. was 30 and 41 mg./100 ml.

*Case 49.*—Female aged 53. Malignant hypertension. Urea concentration, 1.24%. When off treatment the casual blood pressure was in the region of 250/132 and the T.N.P.N. was 52 mg./100 ml. When on treatment with hexamethonium bromide the blood pressure was about 150/100 and the T.N.P.N. was 54, 48, 46, 50, 46, and 40 mg./100 ml.

In a number of instances, microscopical haematuria, albuminuria, and cast excretion have diminished or disappeared coincidentally with blood-pressure lowering, but not to a greater extent than may occur ordinarily with rest.

### Dosage of Penta- and Hexa-methonium Salts

In the course of treatment we have not experienced any difficulty in substituting pentamethonium bromide for hexamethonium bromide in the same dose. Actually formal tests indicate that the hypotensive effect of hexamethonium bromide is usually slightly stronger (Table III). In all instances we have found that when tolerance is acquired to pentamethonium bromide an equivalent degree of tolerance develops for hexamethonium bromide.

In patients who have not had the drug previously, and who are given their preliminary injection in the sitting posture, we find an initial dose of 15 mg. subcutaneously is usually sufficient to cause a considerable fall in the blood pressure when that is high, and about a third of the patients so tested, especially women, have to lie down for a short time corresponding to the trough of the blood-pressure fall. The response to later doses shows the effect of habituation to the action of the drug, so that 250 mg. per injection may have no greater effect than was initially produced by 15 mg.

We wish to stress the great importance, with these drugs, of starting with small doses, as even 15 mg. may have a large effect; but, administered in the sitting posture, there is an added factor of safety, because if the blood pressure falls excessively a change to the horizontal posture will restore the pressure towards normal. In a patient on a salt-free diet 15 mg. may be rather a substantial initial dose, though there will be little trouble if the patient lies flat. Patients with congestive heart failure may get an excessive response, and orthopnoea contraindicates use of the horizontal posture. We have had substantial blood-pressure falls from 5 mg. subcutaneously in a patient with congestive heart failure on a restricted intake of salt. Advantage of a salt-poor diet may be taken in treatment. It economizes in the use of the drug, makes oral administration more effective, and may further supplement the blood-pressure fall in a small proportion of cases by inducing a fall due to the salt-free diet itself. In the case of oral therapy the risk of bromism must be kept in mind.

### Conclusions

When a suitable technique of administration is employed penta- and hexa-methonium salts appear to be most effective and generally applicable hypotensive agents.

We hold most strongly to the view that the extent of the benefits to be derived from penta- and hexamethonium bromides has not been explored unless the method of administration of these substances is one which leads to and maintains a substantial blood-pressure reduction in many classes of case to near normal levels, and for an appreciable proportion of the day and night. With oral dosage this is not always possible after tolerance has developed.

Blood-pressure reduction by penta- and hexamethonium salts has been associated with unmistakable clinical improvement as witnessed by the relief of dyspnoea, pulmonary congestion, headache, papilloedema, and retinal exudates, in the course of treating 53 severe hypertensive patients (including 11 with malignant hypertension) for periods of 1 to 14 months, with one death from cerebral haemorrhage.

Great blood-pressure reductions may be inadvisable in patients with much cerebral or coronary sclerosis. The selection of cases, and the decision on how much blood-pressure reduction should be effected, therefore requires care. For these reasons, and for others set out in the text, treatment must be individualized and controlled by measurements of the blood pressure before administration of the drugs and during the trough of the blood-pressure fall which they induce.

Attempts at treatment which do not take account of individual responsiveness to the drugs, postural

hypotension, the effect of salt intake, the acquisition of tolerance, and numerous other factors will flounder between the dangerous and the ineffectual.


### Summary

There is a close similarity in the hypotensive effects of penta- and hexa-methonium bromides, though formal tests show that hexamethonium bromide is usually slightly stronger in action. We have experienced no difficulty in interchanging these substances at approximately the same level of subcutaneous dosage.

Falls in blood pressure following penta- or hexa-methonium injections are influenced by posture, being greater as the patient approaches the vertical.

Under comparable conditions patients with the higher pressures tend to have the greater blood-pressure falls after hexamethonium bromide injections.

Following sufficiently large injections of these methonium halides, the casual blood pressure falls below the original level of the basal blood pressure, and may be well below this level even in the horizontal posture.

The effects of penta- and hexa-methonium injections on the pulse rate are not constant, but usually as the blood pressure falls the pulse rate increases. This statement applies to the blood-pressure changes induced by changes in posture.

Sensitivity tests to hexamethonium bromide have been carried out in 150 cases of high blood pressure, including 72 cases of fixed and 15 labile types of essential hypertension; 11 following sympathectomy; 11 patients with malignant hypertension; 21 with hypertension following pregnancy toxaemia; two with acute pregnancy toxaemia; 10 with impairment of renal function following surgical disorders of the kidney or nephritis; one case of hypertension associated with polycythaemia; and seven cases of miscellaneous aetiology. Poor response to penta- or hexa-methonium salts has so far been restricted to certain cases of renal damage; other cases with renal damage showed good blood-pressure falls. Fifty-three of the more severe cases were treated, and we have been able to maintain a substantial measure of control over the blood-pressure level.

On the basis of 150 test doses and treatment of 53 cases we would judge that, apart from some of the cases with impairment of renal function, almost all hypertensives can have their blood pressure controlled by these drugs. Among those with impaired renal function the four selected for treatment were readily brought under control without deterioration in their renal excretory capacity as judged by the T.N.P.N. estimations.

Repeated administration gives rise to considerable tolerance, such that 5 or 10 times the original dose may be required to produce the same effect. The acquisition of tolerance to hexamethonium bromide conveys an equivalent degree of tolerance to pentamethonium bromide, and vice versa.

Following repeated administration of penta- or hexa-methonium salts, patients who at the outset exhibit symptoms such as faintness on blood-pressure reduction usually become more tolerant of the lower blood-pressure levels.

The hypotensive actions of penta- and hexa-methonium salts are enhanced on a salt-poor diet (0.2 g. of sodium in 24 hours) to such a degree that dangerous reactions may occur if the effects of this potentiation are not allowed for in determining dosage.

Hypertensive headaches can be relieved in most patients.

The relief of signs and symptoms, when present, in cases treated over a period of months was prompt and striking. Particular reference has been made to the marked improvement of dyspnoea under treatment, and to the disappearance of papilloedema and retinal exudates. Pulmonary congestion disappeared, and there are indications of reduction in heart size and electrocardiographic improvement.


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#### REFERENCES


Addis, T. (1922). *Arch. intern. Med.*, **29**, 539.
Alam, G. M., and Smirk, F. H. (1943). *Brit. Heart J.*, **5**, 152.
Arnold, P., Goetz, R. H., and Rosenheim, M. L. (1949). *Lancet*, **2**, 408.
—— and Rosenheim, M. L. (1949). Ibid., **2**, 321.
Balaban, I. E., Levy, M. B., and Wilde, B. E. (1949). *J. Pharm. Pharmacol.*, **1**, 603.
Barlow, R. B., and Ing, H. R. (1948a). *Nature, Lond.*, **161**, 718.
—— —— (1948b). *Brit. J. Pharmacol.*, **3**, 298.
Burt, C. C., and Graham, A. J. P. (1950). *British Medical Journal*, **1**, 455.
Campbell, A., and Robertson, E. (1950). Ibid., **2**, 804.
Davison, M. H. A. (1950). *Lancet*, **1**, 252.
Frankel, E. (1951). Ibid., **1**, 408.
Hunter, A. R. (1950). Ibid., **1**, 251.
Kilpatrick, J. A. (1948). *Brit. Heart J.*, **10**, 48.
Locket, S. (1951). *Lancet*, **1**, 473.
Paton, W. D. M., and Zaimis, E. J. (1948a). *Nature, Lond.*, **161**, 718.
—— —— (1948b). Ibid., **162**, 810.
—— —— (1949). *Brit. J. Pharmacol.*, **4**, 381.
Restall, P. A., and Smirk, F. H. (1950). *N.Z. med. J.*, **49**, 206.
Saville, S. (1950). *Lancet*, **2**, 358.
Smirk, F. H. (1944). *Brit. Heart J.*, **6**, 176.
—— (1949). *British Medical Journal*, **1**, 791.
—— (1950a). *N.Z. med. J.*, **49**, 637.
—— (1950b). *Lancet*, **2**, 477.
—— (1951). Ibid., **1**, 346.
Turner, R. (1950). Ibid., **2**, 353.
—— (1951). Ibid., **1**, 408.


# BLOOD-GROUP FACTORS AND PHYSIOLOGICAL ICTERUS


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Ever since the pioneering work of Yllpö (1913) and Hirsch (1913) it has been recognized that the icterus index of the serum of newborn infants is higher than the values considered normal for adults. Moreover, in most infants the icterus index rises during the first few days of life, not infrequently with resulting noticeable jaundice of the skin and mucous membranes. Most workers (Weech, 1947) consider that physiological jaundice is due to functional immaturity of the liver at birth. However, the course of the syndrome resembles so closely the course of erythroblastosis caused by mild sensitization to the Rh factor that the possibility has to be considered that physiological icterus may have a similar pathogenesis. For example, sensitization to the A and B agglutinogens has been shown (Halbrecht, 1944; Polayes and McNally, 1948; Wiener *et al.*, 1949) to be a not uncommon cause of a relatively benign form of icterus occurring in the newborn infant which has been designated as icterus praecox by Halbrecht (1944). Similarly it is possible that the benign syndrome of physiological icterus may be the result of some antigen-antibody reaction. Although

several studies have already been published on the blood-group factors in relation to physiological icterus (Lenart and Biro, 1929), a new study including the more recently discovered Rh-Hr blood types seemed in order, if only to exclude the A-B-O groups and Rh-Hr types as bearing a relation to the syndrome. In this paper we shall present studies on the icterus index, red-cell count, and haemoglobin concentration, as well as the A-B-O groups and Rh-Hr types, on 21 randomly selected newborn infants.

## Materials and Methods

The babies studied were all newborn infants delivered by the obstetrical service at the Jewish Hospital, the majority being members of the negroid race. There were no "premature" babies in the group, all weighed over 2,500 g., and all had been delivered close to term. A sample of the baby's blood for typing was obtained from the umbilical cord at birth, and blood from the mother was usually obtained on the following day. On every day thereafter for the first five days of life a sample of the baby's blood was obtained from the femoral vein and mixed with oxalate as for the Wintrobe–Landsberg sedimentation test. The A-B-O and M-N type and the Rh-Hr type of every baby and its mother were determined in the usual manner. The icterus indices were determined on the oxalated plasma by the acetone method, and red counts

TABLE I.—*Cases in which the A-B-O Groups and Rh Factor of Mother and Baby were Compatible*

| Case No. | Blood Types | | Type of Test | Age of Baby (Days) | | | | |
|---|---|---|---|---|---|---|---|---|
| | Mother | Baby | | Cord Blood | 1 | 2 | 3 | 4 |
| 1 | $OMNRh_2Rh_o$ | $OMNRh_1rh$ | I.I. | 8 | 38 | 38 | — | 32 |
| | | | Hb | — | 112 | 113 | 115 | 113 |
| | | | R.B.C. | — | 5·94 | 5·68 | 5·79 | 5·74 |
| 2 | $OMRh_o$ | $OMRh_o$ | I.I. | 4 | 8 | 8 | 8 | 8 |
| | | | Hb | — | 107 | 111 | — | — |
| | | | R.B.C. | — | 5·45 | 5·59 | — | — |
| 3 | $A_1MNrh$ Anti-Rh absent | OMNrh | I.I. | 10 | 16 | 16 | | |
| | | | Hb | — | 100 | 103 | | |
| | | | R.B.C. | — | 4·69 | 4·72 | | |
| 4 | $ONRh_o$ | $OMNRh_o$ | I.I. | 10 | 16 | | 16 | |
| | | | Hb | — | 115 | | 117 | |
| | | | R.B.C. | — | 5·70 | | 5·86 | |
| 5 | $OMNRh_1rh$ | $OMNRh_1rh$ | I.I. | 6 | 16 | 18 | 12 | 16 |
| | | | Hb | — | 105 | 105 | 126 | — |
| | | | R.B.C. | — | 5·3 | 5·22 | 5·82 | — |
| 6 | $ONRh_o$ | $OMRh_o$ | I.I. | 10 | 36 | 48 | 100 | |
| | | | Hb | — | 117 | 117 | 117 | |
| | | | R.B.C. | — | 5·71 | 5·58 | 5·59 | |
| 7 | $OMNRh_o$ | $OMNRh_o$ | I.I. | 16 | 48 | | | |
| | | | Hb | — | 128 | | | |
| | | | R.B.C. | — | 5·34 | | | |
| 8 | $A_2Nrh'rh$ Anti-Rh absent | $ANrh'rh$ | I.I. | 20 | 24 | 44 | | |
| | | | Hb | — | 97 | 95 | | |
| | | | R.B.C. | — | 4·36 | 4·35 | | |
| 9 | $A_2MNRh_1rh$ | $A_2MNRh_1rh$ | I.I. | 14 | 32 | 40 | 48 | 46 |
| | | | Hb | — | 115 | 110 | 110 | — |
| | | | R.B.C. | — | 5·93 | 5·72 | 5·74 | — |
| 10 | $AMRh_2rh$ | AMNrh | I.I. | — | 20 | 24 | 21 | 32 |
| | | | Hb | — | 95 | 97 | — | 99 |
| | | | R.B.C. | — | 4·92 | 5·63 | — | 5·23 |

I.I. = icterus index; Hb = haemoglobin concentration; 100% = 14 g./100 ml.; R.B.C. = red cell count in millions per c.mm.

TABLE II.—*Cases in which the Baby's A-B-O Group and/or Rh-Hr Type was Incompatible with that of the Mother*

| Case No. | Blood Type | | Type of Test | Age of Baby (Days) | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mother | Baby | | Cord Blood | 1 | 2 | 3 | 4 | 5 |
| 11 | $BMRh_2Rh_o$ | $A_1MRh_2Rh_o$ | I.I. | 6 | 8 | 16 | 14 | | |
| | | | Hb | — | 106 | — | — | | |
| | | | R.B.C. | — | 5·36 | — | — | | |
| 12 | $BMRh_1rh$ | $BMRh_1Rh_2$ | I.I. | 4 | — | 8 | 8 | | |
| | | | Hb | — | 110 | 108 | 110 | | |
| | | | R.B.C. | — | 5·94 | 5·40 | 5·47 | | |
| 13 | OMrh Anti-Rh absent | $OMNRh_o$ | I.I. | 12 | 20 | 44 | 44 | 48 | 44 |
| | | | Hb | — | 110 | 112 | 107 | 107 | 106 |
| | | | R.B.C. | — | 5·51 | 5·31 | 5·34 | 5·34 | 5·32 |
| 14 | ANrh Anti-Rh absent | BMNrh | I.I. | 8 | 36 | 32 | 46 | 42 | |
| | | | Hb | — | 114 | 116 | 114 | 110 | |
| | | | R.B.C. | — | 5·73 | 5·81 | 5·79 | 5·58 | |
| 15 | $OMNRh_1rh$ | $MNRh_o$ | I.I. | 12 | 16 | 12 | | | |
| | | | Hb | — | 92 | 93 | | | |
| | | | R.B.C. | — | 4·14 | 4·16 | | | |
| 16 | $A_1MRh_1rh$ | $A_1MNRh_2$ | I.I. | 12 | 24 | 24 | — | 48 | |
| 17 | $OMNRh_1rh$ | $AMNRh_o$ | I.I. | 4 | 4 | 8 | 10 | 8 | |
| 18 | $OMRh_1^wRh_1$ | $AMNRh_1^wRh_1$ | I.I. | 12 | 20 | 24 | 32 | 36 | |
| 19 | $OMNRh_o$ | $OMNRh_1h$ | I.I. | 8 | 16 | 32 | 32 | 32 | 32 |
| | | | Hb | — | 88 | 88 | 103 | 95 | 95 |
| | | | R.B.C. | — | 4·64 | 4·73 | 5·53 | 4·93 | |
| 20 | $ONRh_1rh$ | $ANRh_1rh$ | I.I. | 14 | 32 | 40 | 48 | | |
| | | | Hb | — | 106 | 104 | 103 | | |
| | | | R.B.C. | — | 5·62 | 5·43 | 5·42 | | |
| 21 | $ANRh_2rh$ | $ABMNRh_o$ | I.I. | — | 14 | 18 | 21 | 32 | |
| | | | Hb | — | 110 | 110 | 117 | 106 | |
| | | | R.B.C. | — | 5·73 | 5·74 | 4·6 | 5·2 | |

and haemoglobin determinations were carried out on the daily samples of the oxalated blood. Tests for Rh antibodies were made on the serum of all mothers found to be Rh-negative.

### Results

The cases were divided into two categories depending on whether the A-B-O group and the Rh types were compatible or incompatible with those of the mother, and the results are summarized in Tables I and II. As will be seen, the average icterus index of the cord serum for the group with compatible blood types was 10.8 units, as compared with the average of 9.2 units for the group with incompatible blood types. In most babies of both groups the icterus index rose immediately after birth, and at the highest point in the compatible group the average icterus index was 36.8 units, in comparison with an average at the highest point of 30.9 for the incompatible group.

These results indicate that the high icterus index of the cord serum and the rise which occurs in the neonatal period are not ascribable to any incompatibility involving the A-B-O groups or Rh types. In accordance with the previous observations (Weech, 1947) the values of the blood counts and haemoglobin determinations remained constant from day to day, indicating that the rise in icterus index was not due to haemolysis.

### Comment

Inadequacy of the excretory function of the liver has been shown to be one of the phenomena associated with physiological icterus. The cause for this malfunction has not been determined, though most workers in the field have ascribed it to "immaturity" (Weech, 1947). Because erythroblastosis foetalis is also attended by a marked diminution in the excretory capacity of the liver, Wiener (1951) has postulated a pathogenesis for physiological icterus on an analogous basis. Examination of women at term demonstrates the constant presence in their serum of auto-antibodies in tests carried out at ice-box temperature, especially when enzyme-treated test cells are used. Almost invariably the antibodies are of the univalent variety, so they are presumably capable of traversing the placental barrier and coating the foetal red blood cells. As in the case of mild Rh sensitization, the auto-antibodies derived from the maternal circulation are only occasionally demonstrable free in the cord serum, but the practically universal occurrence of hyperbilirubinaemia in the newborn infant could be explained by the universal occurrence of auto-antibodies in the maternal blood.

One of us (A. S. W.) has further postulated that, since the antibodies are of the cold variety, the cooling of the baby's skin that attends his birth brings about clumping of the coated red cells and acts as the trigger mechanism that sets off the explosion that is physiological icterus. The high incidence of icterus in premature infants, with their poor temperature control, may have a similar explanation, although here developmental immaturity also has great plausibility.

We have recently encountered a case in which an expectant mother was found on antenatal testing to possess cold antibodies in her serum with a titre approximately three times as high as the upper limit found in other mothers. The baby born to this mother developed mild jaundice and anaemia, the haemoglobin dropping to 65% by the time the baby was 3 weeks old. No other cause for the anaemia could be demonstrated. As the titre of cold antibodies has been shown to be elevated in cases of atypical pneumonia and infectious mononucleosis, a search is being made for cases in which pregnant women had these ailments shortly before term.

### Summary

Studies of the A-B-O groups and Rh-Hr types revealed no relationship between these blood factors and the occurrence of physiological icterus in the newborn infant. The average icterus index of the cord serum in babies with compatible and incompatible blood types did not differ, being 10.8 and 9.2 units respectively. At the peak of the hyperbilirubinaemia the values were 36.8 and 30.9 units respectively. There was no fall in red blood cell count or haemoglobin concentration accompanying the rise of icterus index. The possible relationship of auto-antibodies to the syndrome of physiological icterus is discussed.

We wish to express our appreciation to Mrs. Elaine Rieders and Miss Barbara Didio for the performance of the blood counts and the icterus index determinations.

#### REFERENCES

Halbrecht, I. (1944). *Amer. J. Dis. Child.*, **68**, 248.
Hirsch, A. (1913). *Z. Kinderheilk.*, **9**, 196.
Lenart, G., and Biro, S. (1929). *Jb. Kinderheilk.*, **124**, 77.
Polayes, S. H., and McNally, J., jun. (1948). *Amer. J. clin. Path.*, **18**, 375.
Weech, A. S. (1947). *Advances in Pediatrics*, **2**, 346. Interscience Publishers Inc., New York.
Wiener, A. S. (1951). *British Medical Journal*, **1**, 435.
—— Wexler, I. B., and Hurst, J. G. (1949). *Blood*, **4**, 1014.
Yllpö, A. (1913). *Z. Kinderheilk.*, **9**, 208.

## ANGIOCARDIOGRAPHY IN CONGENITAL HEART DISEASE

### ANAESTHESIA AND TECHNIQUE

BY

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Kreutzer *et al.* (1950) state that "angiocardiography is simple and harmless so far as our experience shows." The results from a series of 172 cases of angiocardiography performed for congenital heart disease at Guy's Hospital make it impossible to agree with this statement.

### Literature

Forssmann (1929) was the first to introduce a catheter into the heart (his own) and also to inject a dye (iodoxyl *B.P.*, "uroselectan" 35–50%), but it was not until 1937 that the first *clear* view of the right side of the heart and pulmonary arteries in man was shown by Castellanos *et al.* (1938a). They were unable to show the left side of the heart and aorta, because of the poor contrast medium used. In the following year Robb and Steinberg (1939), using "diodrast" 70% (diodone; the diethanolamine salt of 3,5-diiodo-4-pyridone-N-acetic acid, containing 49.8% iodine), showed the left side of the heart and aorta as well. Their technique, or some modification of it, is the one most commonly used to-day. In these investigations general anaesthesia seems to have been used very infrequently.

Kreutzer and his colleagues carried out their investigations entirely on infants and children without any form of general anaesthesia. They used diodone 75% as the contrast medium in doses of 10 ml. for the

newborn, 12 ml. up to 3 months, 15 ml. up to 1 year, and then 1.5 ml. per kg. of body weight for any child over 1 year. The injection was made intravenously through a procaine weal without exposing the vein. In performing angiocardiography in over 400 cases they had only one death—in an infant with complete transposition of the great vessels. The infant died with high temperature and convulsions 12 hours after injection of the contrast medium.

Castellanos *et al.* (1938b) also carried out their investigations on infants and children. They did not use general anaesthesia, but they realized that complete immobilization of the infant was necessary in order to obtain good angiocardiograms. At first prevention of movement was carried out by manual restraint, but it had the disadvantage that many assistants were required. In order to overcome this, they constructed a device called an "immobilizer," which was made in two sizes —for infants and older children. The contrast medium was injected through a cannula after exposing the vein under local analgesia.

Robb and Steinberg (1939) carried out 238 injections on 127 patients aged between 16 and 74 years. No general anaesthetic was administered, but in cases of "extreme nervousness" the patients were premedicated with a barbiturate. The only other pre-operative measure was to ensure that the stomach was empty. With the patient in the sitting position, the diodone (25–45 ml.) was given with the arm abducted.

Since that time Dotter and Steinberg (1949) have performed angiocardiography in over 1,000 patients without a fatality. Most of these were carried out according to the original technique described by Robb and Steinberg, except that in the last 448 injections, "neoiopax" 75% (sodium iodomethamate) was used as the contrast medium.

Under local analgesia Chavez *et al.* (1947) exposed the external jugular vein, and introduced a rubber catheter (size 12–14) into the right atrium or ventricle. They used 50–90 ml. of diodone as the contrast medium. They report only one death, which occurred after their paper was written.

Anstruther Smith (1950) seems to have been the first to report a series of cases (40) in which general anaesthesia was used. He considers that a general anaesthetic is essential for all children under 5 years and probably up to the age of 12. In his series, cardiac catheterization was performed first, and the contrast medium injected through the catheter after the latter had been withdrawn so that only a few inches remained in the vein. His patients were premedicated with pentobarbitone ("nembutal"), 0.6 gr. per stone (6 mg. per kg.) body weight, and atropine, 1/150 gr. (0.43 mg.), 45 minutes pre-operatively. Anaesthesia was induced with thiopentone and maintained with intermittent injections of the same drug. In a few of his cases angiocardiography alone was performed. These children received the same premedication as above, and anaesthesia was induced and maintained with "trilene" (trichlorethylene) and oxygen through a Boyle machine.

Lee (1950) advises the use of nitrous oxide, oxygen, and trilene for angiocardiography.

## Present Investigation

In this series of 172 patients most have suffered from cyanotic congenital heart disease, though a few have been acyanotic. In 115 cases angiocardiography was performed under general anaesthesia and in the remaining 57 under local analgesia with adequate premedication. The ages of these patients ranged from 3 to 37 years. Most children under the age of 12 received general anaesthesia, but the older patients did not require it. In this series three patients died on the table—two while under general anaesthesia and one who received local analgesia only. A fourth patient died immediately on arrival in the ward. A further patient—a child aged 3—developed signs of cerebral anoxia, but finally recovered sufficiently to return home. Angiocardiography was performed by Mr. I. M. Hill in 121 cases. In the remaining 51 cases it was carried out by Mr. Lawrence Whytehead.

### Technique

The conscious patient is placed in the recumbent position on a special *x*-ray table designed by Hills (1948). On this table 10 exposures are taken in 10 seconds. The surface of the table is 5 ft. (152 cm.) above ground-level, and this tends to make induction of anaesthesia inconvenient; the younger patients therefore are anaesthetized on an ordinary theatre trolley and then transferred to the table.

Originally the young patients were premedicated with pentobarbitone, 0.5 gr. per stone (5 mg. per kg.) of body weight orally 1½ hours pre-operatively and atropine 1/100 gr. (0.65 mg.) 30 minutes pre-operatively. This method of sedation proved unsatisfactory, as cases occurred in which the children were awake on arrival in the *x*-ray department, and it was felt that the small children should not be alarmed in any way. The premedication was therefore changed to rectal thiopentone in a dosage of 1 g. per 50 lb. (22.7 kg.) body weight and atropine 1/100 gr. (0.65 mg.) half an hour pre-operatively. Rectal thiopentone in this dosage was not found to be too depressing even to the younger and more ill patients, and it was much more constant in action. The conscious patient is premedicated with pentobarbitone and atropine on the same scale of dosage as for children, with a maximum of 4.5 gr. (29 mg.) of pentobarbitone.

More recently, all patients have received a test dose of quinidine, 1½ gr. (0.1 g.), and, provided no reaction —for example, nausea, headache, or tinnitus—occurs, quinidine 3–5 gr. (0.2–0.32 g.) is given pre-operatively as a prophylactic against arrhythmias. It is administered either as a divided dose four hours and again two hours pre-operatively, or as a single dose two hours before operation. The dosage, and whether it is given once or twice pre-operatively, depend upon the age, weight, and size of the child. A test dose of diodone in the form of a tablet is given to all patients the day before operation. If no stomatitis develops the patient is considered to be not sensitive; transient urticarial rashes occur very occasionally, but, so far, sensitivity to this drug has not been observed.

In the early cases in the series anaesthesia was maintained with nitrous oxide, oxygen, and trilene through a Boyle machine. But this method was discontinued after the death of a girl aged 12 immediately on her return to the ward. It was realized that a large number of these children were extremely grave anaesthetic risks, and that the slightest degree of anoxia must not be allowed to occur. The patients therefore were induced with cyclopropane and oxygen, and also maintained with the same drug through a Coxeter–Mushin

absorber. This method gave a smooth induction with no trace of anoxia. After further experience it was observed that in a number of cases coughing or breath-holding occurred within 2–10 seconds of the introduction of the contrast medium. At times this was undoubtedly due to bronchospasm, because it was impossible to inflate the lungs, though there was no laryngeal spasm (confirmed by direct laryngoscopy). The coughing and breath-holding could not be prevented by increasing the depth of anaesthesia with cyclopropane, so ether is now added after induction with cyclopropane. Provided the level of anaesthesia was carried to that of deep second plane or early third plane with ether, these immediate respiratory complications became much less frequent.

Although cyclopropane and ether are both explosive mixtures, it was felt safe to use them in an *x*-ray department for the following reasons: (1) The gases are administered in a closed circuit. (2) If leakage of explosive mixtures should occur the relative absence of naked flames or sparks in a modern *x*-ray department is unlikely to give rise to an explosion. (3) The anaesthetic apparatus is placed next to the extraction grille of the air-conditioning plant, so that any gases that may have escaped will be removed from the room.

The patient, having been adequately anaesthetized with cyclopropane and ether, is transferred to the special *x*-ray table and the arm is abducted about 30 degrees from the side. A suitable vein is selected, and skin and subcutaneous tissues are infiltrated with procaine 2% in an endeavour to prevent venous spasm. The vein having been exposed, a large cannula of 0.224-mm. internal diameter is inserted. In the very young patients a smaller cannula of 0.148-mm. bore may have to be used. The cannula is connected to a 100-ml. transfusion syringe with a three-way tap. The syringe contains a "perspex" disk valve which enables normal saline to be separated from the contrast medium. The advantage of this arrangement lies in the fact that after the diodone has been given it is immediately washed through with about 20 ml. of saline. When the syringe has been connected to the cannula, having been partially filled with normal saline, 10–20 ml. of saline is injected to ensure that there is a free flow. The required quantity of diodone 70% is drawn into the syringe and, with the arm abducted to about 90–100 degrees, the injection is made as quickly as possible. The quantity of diodone used was calculated on the aggregation of several factors —for example, weight, size, age, physical development, and general condition of the child (I. M. Hill, 1950, personal communication). But more recently Whytehead has calculated the diodone requirements on a basis of 1.2 ml. per kg. of body weight. He has also introduced various modifications to the technique previously employed.

As soon as the cannula had been inserted a solution of procaine 0.2% in dextrose 5% is given by the drip method in order to reduce myocardial irritability and bronchial secretions. While the procaine is flowing at a rate of 10–20 mg. a minute (depending upon the weight of the patient) blood-pressure recordings are taken at one-minute intervals for four or five minutes. A fall of blood pressure amounting to 10–20 mm. Hg may be expected, but at the end of four or five minutes it is usually found to be steady at this lower level. It is now considered safe to inject the diodone solution provided the E.C.G. tracing is satisfactory. If, however, the blood pressure should continue to fall or a gross drop of blood pressure should occur immediately and no improvement take place on slowing the rate of flow of procaine, then the angiocardiogram ought to be abandoned. So far we have not had to resort to this in any of our cases.

The contrast medium having been injected, blood-pressure recordings are still taken at intervals of a minute. An immediate marked fall in blood pressure usually occurs, but within one to two minutes it starts to rise and in five to eight minutes is usually slightly above the reading taken immediately before the injection of diodone. Continuous blood-pressure records were taken by Howarth (1950), who found a similar fall in blood pressure in all her cases. If, however, the rise in blood pressure does not start within two minutes resuscitative measures should be introduced. Oxygen 100% is given and methylamphetamine hydrochloride (methedrine) 5–10 mg., intravenously. If there is no improvement preparations should be made for cardiac puncture and cardiac massage, a stop-watch being used to time events. Intracardiac injections of procaine 5% for ventricular arrhythmias and calcium chloride 1% to improve myocardial tone may have to be given. Immediately after the injection of diodone, procaine 0.2% is given in the same dosage as above until the blood-pressure recordings are satisfactory. E.C.G. tracings are taken throughout the investigation, starting immediately after induction of anaesthesia.

In only one case out of 90 in which E.C.G. tracings have been recorded has angiocardiography been abandoned, and this was due to a 2 to 1 heart-block, which persisted in spite of removal of cyclopropane from the anaesthetic mixture, the administration of intravenous procaine, and atropine. Nodal rhythm is often seen before the diodone injection, and after the injection S–T depression and abnormalities of conduction leading to incomplete heart-block are revealed. These appear to be expressions of coronary insufficiency. The patient, with oxygen through a B.L.B. mask, is then returned to the ward under the care of the anaesthetist and is placed in an oxygen tent for the next three to twelve hours.

### Complications

Secretions in the tracheo-bronchial tree are not always inhibited satisfactorily by atropine. Their presence greatly enhances the danger of laryngeal spasm, which on this type of patient may produce sufficient anoxia to endanger life. Either angiocardiography must be abandoned or a further dose of atropine 1/100 gr. (0.65 mg.), must be injected intravenously by the anaesthetist before giving the anaesthetic. A sucker should always be available during angiocardiography.

Breath-holding due to bronchospasm or laryngospasm may occur when the diodone enters the pulmonary vessels; liability to this can be reduced to a marked degree by adequate depth of anaesthesia with ether, which is, of course, a bronchodilator. Intravenous procaine may also play some part in preventing bronchospasm. If the apnoea is due to bronchospasm, oxygen 100% must be administered, while the spasm itself might be relieved by an antihistamine drug, such as "benadryl" (diphenhydramine hydrochloride) or "anthisan" (mepyramine maleate), given intravenously. Up to this time we have had no experience of the use of the antihistamine drugs. If laryngeal spasm has occurred a gum-elastic catheter should be pushed gently through the vocal cords and oxygen given immediately. The delay in waiting for the laryngeal spasm to pass may

give rise to such a degree of anoxia that permanent cerebral damage occurs. Laryngeal spasm may also result from reflex vomiting during return to consciousness; the patient must therefore be kept under the observation of the anaesthetist until consciousness is regained.

Vomiting may continue for 24 hours after angiocardiography. This is probably due to the diodone, as it occurs in patients who have not been given a general anaesthetic.

## Discussion

Statements have often been made which suggest that investigation by angiocardiography is without danger to the patient. There are two reasons for these statements. First, if investigations are carried out on comparatively fit patients the mortality rate is extremely low. Secondly, there is no doubt that, however well a general anaesthetic is administered, danger to the patients is greatly increased if they are "poor risk" subjects. Therefore in these extremely ill children suffering from congenital heart disease it is best to avoid a general anaesthetic if possible. This can be done in a co-operative well-premedicated child of about 9 years; but below this age the child tends to be uncooperative if it is sufficiently premedicated to remove all apprehension. Also, the sensation of heat, headache, and vomiting or nausea after injection of diodone may make the young child move while the *x*-ray films are being taken. Normal respiration in the anaesthetized child does not interfere with the films, but the conscious subjects are asked to hold their breath following injection.

A sign of grave prognostic significance is a history of cyanotic attacks or attacks of unconsciousness. All the four children that died had suffered from these attacks, as did the small child of 3 who suffered from cerebral anoxia. Four seconds after the injection of diodone this child developed bronchospasm, which lasted about 60 seconds. Spontaneous respirations then started, but after a few breaths apnoea occurred again. Artificial respiration with oxygen 100% was begun, and after about five minutes spontaneous respirations which were slow and shallow returned; this type of respiration continued for the next few hours while the patient was in an oxygen tent. The child remained in a semi-conscious state for 36 hours and was unable to swallow for 48 hours after angiocardiography.

All patients should be kept in the *x*-ray department for at least 15 minutes after the operation—as the danger period seems to be 30 seconds to 10 minutes after the injection of diodone. In the four fatal cases collapse occurred within this period. The child operated on under local analgesia vomited very shortly after the injection, became unconscious at the same time, and died within 10–15 minutes.

Of the remaining three patients two died early in the series before E.C.G. tracings were routine, but the third case was interesting in that the first sign of any upset was the presence of E.C.G. changes. Six seconds after the injection the child held its breath for about four seconds, but spontaneous respiration then started and the child's colour and pulse were good. Two minutes after the injection the child hyperventilated for 12 breaths; respirations then ceased and the pulse became impalpable. Cardiac massage was started five minutes later, but was of no avail. The E.C.G. tracings were suggestive of a posterior infarct at 30 seconds after the injection; this was followed by disorganized rhythm and finally ventricular fibrillation (G. L. L. Reynolds, 1950, personal communication). The interesting fact about this patient was the presence of marked E.C.G. changes about one and a half minutes before any clinically detectable deterioration occurred.

Since even the slightest degrees of anoxia are probably the gravest dangers that these patients have to face, every effort should be made to prevent the occurrence of oxygen lack. This can be aided by full atropinization (1/100 gr. half an hour pre-operatively to any patient over the age of 1 year), so that secretions from the tracheo-bronchial tree are absent. Although intubation has not been done in any of these cases it seems that this ought to be carried out in order to maintain a perfect airway throughout.

Cardiac catheterization is usually performed some days or weeks before angiocardiography. The complete injection of diodone through our catheters cannot be carried out in 1.5–2 seconds, and therefore it is preferred to inject through a larger cannula. If, however, a particular heart defect or chamber is to be shown the catheter can be placed in that chamber and a small quantity of contrast medium injected satisfactorily.

## Conclusions

A large number of these cases of congenital heart disease are serious anaesthetic risks. Angiocardiography should therefore be carried out in an *x*-ray theatre with full surgical and anaesthetic equipment to deal with any emergency. Pre-operative cyanotic attacks are of bad prognostic significance. The older patients should be premedicated with pentobarbitone and atropine, the younger with rectal thiopentone and atropine. Quinidine and a test dose of diodone should also be given pre-operatively. Cyclopropane, ether, and oxygen, through a cuffed endotracheal tube, form the anaesthetic of choice. Intravenous procaine, both before and after the injection of diodone, should be given through a large cannula inserted into the vein under direct vision. Serial blood pressures and E.C.G. tracings ought to be recorded. The patient must be carefully watched for 15 minutes after the injection; must be under the care of the anaesthetist until consciousness is regained; and must spend the first three to twelve hours post-operatively in an oxygen tent.

I wish to express my thanks to Dr. E. H. Rink, Dr. P. J. Helliwell, and Dr. A. M. Hutton, who have administered a number of the anaesthetics for these cases, and given me their advice and encouragement.

### REFERENCES

Castellanos, A., Pereiras, R., and Garcia, A. (1938a). *Pr. méd.*, **46**, 1474.
—— —— —— and Paussa, A. V. (1938b). *Bol. Soc. cubana Pediat.*, **10**, 217.
Chavez, I., Dorbecker, N., and Celis, A. (1947). *Amer. Heart J.*, **33**, 560.
Dotter, C. T., and Steinberg, I. (1949). *Ann. intern. Med.*, **30**, 1104.
Forssmann, W. (1929). *Klin. Wschr.*, **8**, 2085.
Hills, T. H. (1948). *Brit. J. Radiol.*, **21**, 511.
Howarth, S. (1950). *British Medical Journal*, **2**, 1090.
Kreutzer, R. O., Caprile, J. A., and Wessels, F. M. (1950). *Brit. Heart J.*, **12**, 293.
Lee, J. A. (1950). *A Synopsis of Anaesthesia*, p. 302. Wright, Bristol.
Robb, G. P., and Steinberg, I. (1939). *Amer. J. Roentgenol.*, **41**, 1.
Smith, J. A. (1950). *British Medical Journal*, **1**, 705.

Hampstead Health Institute (see *British Medical Journal*, January 20, p. 111; and May 5, p. 1024) is probably being bought by the London County Council for £10,000 and will be used when the clinic services in the area are increased.

# CONTINUING NURSING CARE FOR THE SMALL INFANT DISCHARGED FROM HOSPITAL

BY

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Discharge home of an infant from hospital necessarily involves a break in the continuity of professional supervision. The break applies less to medical than to nursing supervision. Established custom ensures that the family doctor is advised concerning babies who are being returned from hospital to his care. Continuing medical care is thus favoured. In contrast, arrangements for securing continuing nursing supervision where it is required are less simple. This is true of infants leaving any hospital. The situation arises particularly in the case of the newborn infant discharged from a maternity hospital in certain circumstances. Two examples will suffice: (1) the case of the baby returning home before feeding has been established or before the mother is certain of her desire to feed her baby or confident of her ability to do so; and (2) the problem suddenly presented to the mother by the arrival home of her baby, who has been retained in hospital on account of illness or prematurity.

Discharge of babies in such circumstances involves transfer of considerable responsibility from trained nursing staff to a mother who, however willing, may be understandably anxious. Anxiety not to separate mother from child may on rare occasions contribute to the undesirably early discharge home of a baby. On the other hand, the desire not to impose too great a nursing problem on a mother may result in a baby being detained for an unduly long period in hospital. These and similar difficulties are less likely to arise if the households to which babies are being returned are assured of nursing assistance and guidance. The assistance required, for a temporary period at least, calls for more time and personal attention than the district midwife or health visitor can readily give in the course of her normal routine duties. Nor is this of a nature which every busy family doctor can reasonably be expected to give with the frequency or in the detail desirable.

The problem resolves itself into the provision for selected infants and for a limited period of the services of a nurse who is skilled in the care of infants and who, at the same time as helping the family doctor, will serve as a link between the hospital and domiciliary services.

This article is intended to describe a year's experience of a limited experiment designed to deal with the problem described above. Those taking part in the experiment include members of the staff of the infant-welfare departments of the City of Leeds and of the West Riding County Council, and the Leeds Maternity Hospital.

## Arrangements with the City of Leeds

The first phase of the experiment took the form of arrangements which were agreed between the City of Leeds Health Department and the Leeds Maternity Hospital after previous consultation with the senior obstetrical staff and matron of the hospital, and which had particular reference to premature babies. In accordance with these arrangements, the hospital informs the health department concerning babies who are due for early discharge and who are considered to need continuing nursing supervision. This advance information is telephoned by the resident paediatric registrar to the supervisor of midwives. Selection of infants for special follow-up nursing care is made by the visiting paediatrician to the hospital. On receipt of a telephone request from the registrar, the supervisor of midwives then allocates responsibility for the baby in question to one of her staff. Nearly all the cases are allocated to one of a team of special nurses who are also trained midwives employed whole-time on follow-up care of infants included in the scheme and who have had special experience in the domiciliary care of premature and ailing newborn infants.

When informed of a new case the nurse visits the maternity hospital. There she is introduced to the mother of the baby by the lying-in ward sister, and has explained to her by the paediatric registrar and ward sister the clinical or other circumstances which have prompted a request for the baby to be specially followed up. In the event of the mother having been discharged before the baby, arrangements are made for the mother to revisit the hospital at the same time as the special nurse.

At an early date the nurse visits the home to which the baby will be soon returning. There she satisfies herself that all is in readiness and that no essentials are lacking. The special nurse knows in advance the day on which the baby will be discharged from hospital and makes a point of visiting the household a few hours after the baby's arrival home. After she has seen the baby and given the mother any necessary help the nurse telephones the family doctor, advising him concerning the baby's return home and general condition. The doctor receives additional information from the paediatric registrar, who as a routine in all such cases sends a letter summarizing clinical events during the time the baby was in hospital and explaining the reasons why the help of the health department has been enlisted.

The frequency with which the special nurse pays further visits depends upon the baby's progress, upon the needs of the mother for guidance, and upon the wishes of the family medical attendant. Arrangements are invariably made to meet a family doctor's request to see him by appointment. On an average, visits have continued for a period of three to four weeks. At first the visits are daily, or if necessary several times daily. Later they are made at intervals of several days. Exceptionally, visits have continued for longer than four weeks where the baby's progress has been slow, where the mother has had trouble with her breasts, or where for various reasons she has been slow to show ability to look after her infant. Visits cease when the demands on the nurse's time are not in excess of those with which a health visitor can cope. The last visit is made in company with the health visitor, to whom the facts concerning the baby's progress are explained.

Field workers are always in danger of losing contact with their colleagues at the centre. To forestall any such risks periodic meetings are arranged which are attended by the nurses undertaking the follow-up care and by those on the paediatric staff of the maternity hospital. The meetings enable the results of the follow-up care to be assessed, and provide opportunities for the joint discussions of clinical and other problems met with in hospital and on the field.

### Arrangements in the West Riding

Initially, selection of babies was limited to those whose homes were in the City of Leeds. Early results suggested that arrangements might be extended to selected babies born in the Leeds Maternity Hospital and returning to homes outside the city boundary. Not unexpectedly, a county area presented problems of its own. Although relatively small in number, the children involved have returned to homes dispersed over an extensive geographical area. The distances separating the homes from one another and from the maternity hospital have been considerable. It is not often possible for a district midwife or health visitor from outlying districts to visit the maternity hospital. The employment whole-time, on a county basis, of special nurses on follow-up services of the type described in connexion with the county borough of Leeds is seldom practicable. Nor has the practising midwife the time to supervise the nursing care of babies returned from hospital. To meet the county situation the special follow-up visits are undertaken by health visitors.

The resident paediatric registrar at the maternity hospital, having previously telephoned the family doctor, communicates with the county superintendent of health visitors, who is in charge of organized arrangements for the aftercare of children discharged from hospital. This nurse then visits the maternity hospital, sees the mother, and is given first-hand information about the baby by the registrar and ward sister. Subsequently she arranges (through the divisional medical officer) for follow-up care to be undertaken by the appropriate health visitor, to whom she passes on the facts previously obtained from the hospital. In cases of special difficulty the superintendent of health visitors herself visits the home. In all other respects the procedure followed by the county authority resembles that described in connexion with the City of Leeds.

A further although very limited extension of the original experiment developed in rather more fortuitous fashion. At different times two babies were transferred from the maternity hospital to general hospitals in the city for necessary treatment. In both instances, when the time for final discharge arrived, and after consultation with the family doctor, the local health authority was asked to implement nursing follow-up arrangements. This in turn has led to similar approaches being made in the case of a few babies leaving the children's wards of general hospitals after surgical, medical, or dietetic treatment.

### Selection of Babies

To date 225 babies have been provided with follow-up nursing care. Selection is not subject to any rigid rules, but takes account of the physical well-being of the infant, doubts concerning the establishment of appropriate feeding, and home circumstances. Assessment of the baby's condition is based upon daily observations of the developing clinical pattern, and on the findings of repeated complete physical examination. Account is taken of the bearing of such anomalies as cleft-palate or congenital heart on care of the infant during the early weeks after discharge home.

An infant who has survived a clinically violent neonatal course is regarded as suited to a follow-up; so also is a baby with evidence of some localized superficial infection which may be slow to heal if the infant is detained in hospital, but which may be expected to disappear rapidly with removal from a hospital environment. The random examples quoted are not met with often, but illustrate the variety of factors which may influence selection. The two factors of greatest importance in influencing selection are prematurity and incompletely solved feeding problems. Final selection takes place at the cot-side, takes account of the wishes of the mother and the observations of the paediatric registrar and ward sister, and aims at anticipating situations in which the family doctor would appreciate skilled nursing assistance.

### What Are the Advantages of the Arrangements?

Experience over the past year justifies the view that the arrangements are beneficial not only to mother and child but also to those responsible for the professional care of the newborn infant. Some of these immediate benefits may be conveniently summarized as follows:

1. The informal procedure whereby the domiciliary nurse is introduced to the mother by the hospital staff gives to continuity of supervision a live personal touch of infinite value.

2. The hospital midwife finds satisfaction and stimulus in the personal interest shown in her work by her colleagues on district.

3. The nurse working on district is brought in contact with and reminded of the difficulties of nursing the neonate under institutional conditions, and finds a verbal exchange of information given before assuming responsibility for a baby more stimulating and more helpful than facts recorded on prescribed forms.

4. Breast-feeding is often successfully established and maintained in circumstances (delayed lactation, temporary decline of secretion, malformed nipples, etc.) which in the absence of adequate follow-up measures often contribute to natural feeding being wholly discontinued after discharge from hospital and without any professional advice (medical or nursing) being sought.

5. A number of babies who might otherwise be retained in hospital for precautionary observation or minor treatment can be confidently returned home with their mothers.

6. Infants who on account of prematurity, frailty, or illness are detained in hospital after the discharge of their mothers are enabled to return home sooner than would otherwise be the case.

7. The demands on hospital nursing staff are lessened and the pressure on maternity nursery cots is relieved.

8. The attention of mothers is focused on the desirability of continuing medical supervision by the family doctor as a preventive measure.

### Other Considerations

Any arrangements which involve team-work and the linking of hitherto separate or partially separate interests are apt to give rise to misgivings. The local experiment described has been no exception, but so far as we can assess the doubts have been few in number. If they are more numerous than we believe, it is because they have not been brought to our notice. Certainly there have been no complaints from any households. On the

contrary, there have been many unsolicited expressions of appreciation, by mothers and relatives, of the nursing care given in the homes. Lying-in ward sisters have, without exception, welcomed the contact with their colleagues working in the field and are enthusiastic in their encouragement of follow-up care. The enthusiasm of those undertaking the follow-up nursing care is no less than that of the ward sisters.

While it has been relatively easy to gauge the reactions of the nurses, it has been less easy to gauge those of the family doctor. Two instances have occurred of general practitioners objecting to the special visits of the nurse or health visitor. A number have spoken of the value of her help, and, as was to be anticipated, there have been isolated occasions when the nurse's advice has been modified or reversed at the time of the doctor's visit. It need hardly be stated that the medical attendant is looked to for decisions relating alike to treatment of the child or mother. There have been other occasions when the visiting nurse has been instrumental in securing for a baby timely medical advice not thought to be necessary by the parents. On a number of occasions the nurse has been able to secure urgent help necessary to offset in part at least the indirect effects of poverty and slum conditions.

The few misgivings of which we have heard appear to have arisen from suspicions concerning motives rather than from doubts about the working practicability of the arrangements. The arrangements have only one motive—the discharge home, with the minimum of delay, of small babies who are in hospital as a result of illness or of the circumstances of birth. It is implicit in the arrangements that when the family doctor assumes clinical responsibility for these babies he should be enabled to share in the indispensable benefits, known to his hospital colleagues, of having the assistance of a nurse skilled in the observation and in the general management of the small or ailing infant aged only a few weeks. Success is dependent upon careful selection of infants; the skill, knowledge, and personality of those providing the infant-nursing care; and co-operation between the family doctor, the local health services, and maternity hospitals. If this co-operation can be firmly secured the task of hospitals will be lightened, the place of child care in the home will be emphasized, and a further contribution—no matter how small—will have been made to improved prospects of total health in infancy and childhood.

We are indebted for generous co-operation to Sisters G. E. Capewell, A. M. Kelly, M. Pattullo, M. McMackin, and A. H. G. Whitehill, of the Leeds Maternity Hospital; to Miss D. Humphrey, supervisor of midwives, and Sisters D. Booth and B. Chapman, of the City of Leeds Health Department; and to Miss A. Carey, superintendent of health visitors, and the health visitors of the West Riding County Council.

At a meeting of the North of England Section of the Society of Public Analysts in April, Mr. J. G. Sherratt compared the methylene-blue grading test and the plate counts of ice-cream. He said that comparison of the results of the methylene-blue grading test for 1,400 samples of ice-cream from various sources was made with the results of plate counts at 37° C. and 20° C. and the coliform population of the samples. It was concluded that a Grade 1 indication may be accepted with confidence, that about 80% of samples falling into Grade 2 were bacteriologically satisfactory, and that the presumption that samples falling into Grades 3 and 4 are unsatisfactory must be adopted only with considerable reserve.

# CARCINOMA OF THE PROSTATE

## A COMPARISON OF METHODS OF DIAGNOSIS

BY

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The difficulty of making a conclusive differential diagnosis between malignant involvement and inflammatory changes in the prostate gland raises the question of the reliability of the various methods of investigation. The importance of this differential diagnosis becomes all the more evident when it is realized that cancer of the prostate is said to be the commonest carcinoma in the male over the age of 60 years (Hey, 1948). In 1921 the death rate from this disease was 4.18 per 100,000 of the male population, and it had risen in 1930 to 7.55 (Hoffman, 1934). The Registrar-General's Review for 1948 records double the number of deaths from this disease in 1948 than in 1928 (Registrar-General, 1948).

There is a wide divergence of opinion regarding the effect on the expectation of life from the introduction of hormone therapy in a patient with cancer of the prostate; nevertheless it is generally agreed that, whether conservative or radical surgical treatment is to be undertaken, only by early diagnosis can the best results be obtained.

In order to review the reliability of the commoner methods of diagnosis a series of 62 cases (see Table) in

*Cases (62) Suspected of Cancer of Prostate on Rectal Examination*

| | Non-malignant (28) | | | Malignant (34) | | |
|---|---|---|---|---|---|---|
| | No. Examined | Normal | Inconclusive Evidence | No. Examined | Definite Evidence of Malignancy | Inconclusive Evidence |
| Cystoscopy .. .. | 28* | 15 | 9 | 30 | 14 | 16 |
| Radiological examination | 28 | 28 | Osteitis deformans 2 | 34 | Secondaries of bone 15 | 19 |
| Serum acid phosphatase .. .. | 28 | 25 | 3 | 34 | 9 | 25 |
| Test for malignant cells in prostatic secretion or in urine | 28 | 28 | 0 | 32 | 19 | 13 |
| Needle biopsy .. | 19 | 19 | 0 | 21 | 17 | 4 |
| Perurethral biopsy . | 19 | 19 | 0 | 21 | 17 | 4 |

* Four of these patients had carcinoma of the bladder.

which there were strong clinical grounds for suspecting malignant changes in the prostate were investigated and the results compared. Of these cases only 34 had cancer of the prostate.

### Rectal Examination

This had elicited one or more of the following alterations in the gland suggestive of malignant change: (1) increased induration in a part or the whole of the gland; (2) irregularity in the contour of one or both lobes; (3) obliteration of the notch between the seminal vesicles; (4) induration along the lateral ligaments and lymphatics of the gland, especially at the upper pole and the seminal vesicles; (5) loss of the lateral sulcus; (6) increased fixation of the gland on bimanual palpation; (7) the membranous urethra broadened, indurated, ill-defined, and more fixed.

Of the 62 cases 34 were proved to be carcinomatous; of these latter, induration of a part or the whole of the

gland was present in 31, increased fixation in 34, and induration of the lateral ligaments in 22. Of the 28 non-malignant prostatic cases, induration was present in 27, decreased mobility in 24, and extraglandular induration in 11.

### Cystoscopic Examination

Although cystoscopic investigation is considered inadvisable by some urologists (Macalpine, 1949) for fear of disseminating malignant cells, it may provide valuable information, especially regarding lesions primarily of the bladder or urethra but involving the prostate; while the changes in the gland may be evident by the gritty resistance offered to the passage of the cystoscope, the more obvious fixation of the gland, easier identification of induration in the gland by palpation over the instrument, irregularity of the internal urinary meatus, puckering of the mucosa at the apex of the trigone, and the presence of nodules on the floor of the bladder in advanced cases. Of the 30 cases of cancer of the prostate which were cystoscoped, 14 showed a picture strongly suggestive of malignancy, while in 16 the bladder appeared normal. Of the non-malignant cases, 9 showed irregularity or oedema of the bladder floor, 15 were normal, and 4 had carcinoma of the bladder.

### Radiological Examination

This is done to exclude any condition of the prostate or bladder which might cause induration and fixation of the gland and also to detect metastases in the bone, which would denote the late stage of the disease. Of the 34 cases of cancer of the prostate 15 showed secondaries in the bones. The commonest sites were the rami of the pubis and ischium, then the ilium and sacrum, and lastly the lumbar spine. There were two cases of osteitis deformans, which were confirmed by the high level of the alkaline serum phosphatase.

### Serum Acid Phosphatase Estimation

Estimation of the serum acid phosphatase has become a routine procedure since phosphatase was shown to be present in large amounts in carcinomatous prostatic tissue and in its metastases, and that in such cases the serum acid phosphatase might be considerably raised (Gutman and Gutman, 1940). It is generally agreed that readings above 4 K.A. units are suggestive of carcinoma of the prostate, while above 10 K.A. units they are diagnostic (Huggins and Hodges, 1941). The converse, however, does not hold good, for it is usually stated that in only 40% to 50% of cases of cancer of the prostate is the phosphatase level raised above normal. In the present series the serum acid phosphatase was raised in 9 cases to above 4 K.A. units, and in 4 of these it was over 10 K.A. units. Of the 15 cases with secondary deposits in bone 6 showed readings above normal limits.

### Malignant Cells in Prostatic Secretion

The identification of malignant cells in prostatic secretion and in urine as a means of diagnosing cancer of the prostate has been a source of interest for many years. In 1931 Mulholland recorded the presence of clumps of epithelial cells with large acidophilic nuclei in 77% of cases of carcinoma of the prostate. Herbut and Lubin (1947), adapting the technique evolved by Papanicolaou in staining vaginal smears for uterine carcinoma cells and applying it to prostatic secretion, were able to identify the epithelial cells from various parts of the normal lower urinary tract, benign conditions of the prostate, and carcinoma of the prostate gland. The recognition of these cells depends not only on their arrangement in sheets or clumps or as single cells, on the cell outline, on the size of the cells, and on the position and staining of the nuclei, but also on the characteristic colour imparted to the malignant cells by this method of staining. Those authors were able to make a cytological diagnosis of carcinoma in 17 out of 100 patients; 10 of these cases were confirmed histologically and 6 were considered to be reasonably certain on clinical grounds. In a later paper Herbut (1949) reports that neoplastic cells were found in 54 out of 66 cases of known cancer of the prostate. Albers, McDonald, and Thompson (1949), using haematoxylin-eosin staining, found 3 cases of carcinoma of the prostate among 100 patients with a supposedly benign enlargement of the prostate and 13 positive smears in 24 known cases of carcinoma of the gland.

The main objection to this diagnostic method is that prostatic massage might cause a dissemination of cancer cells: this risk is regarded by its advocates as very slight and to be justified by earlier diagnosis. It has been suggested that prostatic secretion may be obtained from the urethra immediately after defaecation, the bladder having previously emptied; while Chute and Williams (1948) report that, by centrifuging the early morning specimen of urine, malignant cells were found in 10 out of 24 cases of known carcinoma of the prostate.

In the present series of 34 cases of cancer of the prostate, malignant cells were identified in 19. In 5 of these cases the finding of malignant cells was the first definite evidence of malignancy. None of the non-malignant cases showed cells suggestive of malignancy, but 13 had numerous pus cells, denoting a chronic imflammatory condition of the gland. The presence of pus cells, however, does not necessarily indicate a benign condition of the prostate, as they were present in 7 of the malignant cases.

### Prostatic Biopsy

Conclusive evidence of the malignancy of the prostate gland can be obtained only by histological examination of tissue removed from the suspected area. Such tissue is obtained by a biopsy needle (Figs. 1 and 2) by perurethral resection, or by excision through the bladder or perineum.

*Needle Biopsy.*—The advantage of this method is that it causes the least amount of discomfort to the patient and of disturbance to the urinary tract, while tissue can be removed from any part of the gland. But the amount of tissue may be small, and considerable experience in sectioning and interpretation is required. The best-known needles are Lowsley's biopsy instrument, Silvermann's needle, and the harpoon types of needle. In 1944 Roth and Turkel modified (Fig. 2) the latter's bone-marrow biopsy needle by increasing its length, and they showed that by inserting this needle in the midline of the perineum, midway between the anus and the bulb of the urethra, it could be directed to any suspected nodule or lobe of the prostate by the left index finger in the rectum. That finger is then hooked over the upper border of the prostate and the gland compressed on to the trephine, which is passed up the needle. By rapid rotation of the trephine a column of tissue over a millimetre in diameter and of the desired length can be removed, and its removal may be facilitated by suction from a syringe exerted through the lumen of the trephine. Haemorrhage is controlled by pressure with the index finger at the point at which the trephine enters the gland or by a

diathermy electrode passed up the needle. This type of needle was found to be the most effective in obtaining adequate pieces of tissue from the prostate gland.

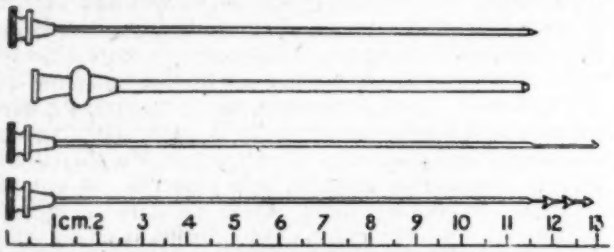


FIG. 1.—Needles designed to combine the tissue-holding action of the harpoon needle with the cutting action of the trephine. The pointed obturator, when in place within the trephine, allows the latter to be inserted through the mid-point of the perineum down to the prostatic capsule. The obturator is removed and the harpoon-like stylet is passed down the trephine into the suspected tissue. By slightly withdrawing the harpoon the tissue is compressed on to the edge of the trephine, which by a rotary cutting action removes a bigger piece of tissue than if the tissue was not compressed. (Made by Messrs. C. Thackray.)

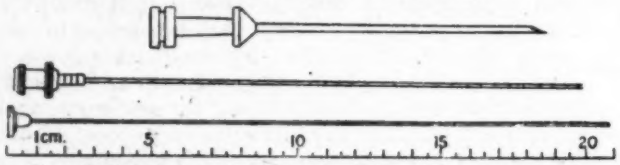


FIG. 2.—The elongated Turkel needle with its obturator in place. The trephine is next to the needle; its length compared with that of the needle and its toothed cutting end are shown. Below is the stylet with which the column of tissue is pushed out of the trephine. (Made by Down Bros. and Mayer & Phelps.)

*Perurethral Biopsy.*—Perurethral resection of the prostate gland by McCarthy's electrotome or Thompson's punch has the advantage of excising large pieces of tissue while at the same time removing bladder-neck obstruction. But biopsy then becomes a major surgical procedure, especially if the tissue under suspicion is situated at the periphery of the gland or in the posterior lobe, which, again, is regarded as the commonest site for early carcinoma of the prostate. The results from perurethral biopsy and Turkel's needle correspond closely. Perurethral resection was carried out in 21 of the 34 malignant cases, and in each instance a needle biopsy preceded the resection; in 17 cases the perurethral fragments showed a carcinoma of the prostate, while in 2 the needle biopsy revealed carcinomatous areas which perurethral section had failed to show. In 2 cases the tissue removed by the needle presented no sign of malignancy when it was evident in the perurethral sections. This discrepancy was mainly due to the fact that a recently sharpened trephine is essential, and this is practicable only if two or more trephines are available—a condition that obtained only during the latter part of the investigation.

## Discussion

Carcinoma of the prostate shows an increasing incidence greater than can be accounted for by the ageing of the population. The gradual onset of symptoms is responsible for the spread of the malignant process beyond the prostatic tissue in 90% to 95% (Barringer, 1935) of cases before diagnosis is made, and the interval between the onset of symptoms and diagnosis has been estimated at 25 months (Wear and Schoenenberger, 1948).

Many authorities believe that hormone therapy has extended life only 18 to 21 months in the majority of cases, while others claim that a large percentage reach the 5-year survival period. It is generally agreed that from 10% to 20% of patients fail to respond to oestrogen, while of those who do react a number rapidly become resistant to hormone therapy. But, whether medical or surgical treatment be adopted, the results will largely depend on how early the diagnosis has been made.

Clinical diagnosis depending on rectal examination has been claimed to be reliable in up to 88% of cases, but in the present series of 62 clinically suspected cases only 34 were proved to be carcinomatous.

Cystocopic examination, although considered inadvisable by some urologists, may be of help in determining the extent of the disease, the induration of the gland, and its fixation, and is especially valuable in excluding diseases of the bladder and urethra which by involving the prostate may simulate carcinoma; four such cases were discovered in this series.

Radiological examination is a routine procedure to exclude those lesions of the bladder and prostate which may cause induration and fixation of the gland and thus simulate a malignant involvement. Secondary deposits in the bones of the pelvis and spine indicate the late stage of the disease. Bony metastases were present in 15 of the malignant cases.

The level of the serum acid phosphatase is a valuable diagnostic measure. It is accepted that readings above the normal limits of 4.0 K.A. units are strongly suggestive of malignancy and are diagnostic when raised above 10 K.A. units; but they are raised in less than 50% of cases of carcinoma of the prostate. In this series they were raised in 9 of the 34 malignant cases.

The identification of malignant cells in the prostatic secretion obtained either by prostatic massage from the urethra immediately following defaecation or by centrifuging the early morning specimen of urine is valuable confirmatory evidence. The reliability of this test is reported as being 84% after massage and 54% in urine. In the present series a positive diagnosis was made in 19 of the 34 cases of carcinoma of the prostate.

The only conclusive evidence of malignant involvement of the gland is by microscopical examination of biopsy tissue removed from the suspected area of the prostate. The most efficient biopsy needle was found to be Turkel's. Perurethral resection provides larger pieces of gland for section and at the same time removes bladder-neck obstruction, but it may be difficult to remove tissue from the periphery of the gland or from the posterior lobe. The results of these two methods of biopsy correspond very closely.

I wish to thank Dr. R. Thomson for his assistance and advice regarding the histology and the identification of malignant cells in the prostatic secretion.

### REFERENCES

Albers, D. D., McDonald, J. R., and Thompson, G. J. (1949). *J. Amer. med. Ass.*, **139**, 299.
Barringer, B. S. (1935). *J. Urol.*, **33**, 616.
Chute, R., and Williams, D. W. (1948). Ibid., **59**, 604.
Gutman, A. B., and Gutman, E. B. (1940). *J. biol. Chem.*, **136**, 201.
Herbut, P. A. (1949). *Amer. J. clin. Path.*, **19**, 315.
—— and Lubin, E. N. (1947). *J. Urol.*, **57**, 542.
Hey, W. H. (1948). In *Textbook of Genito-Urinary Surgery*, edited by H. P. Winsbury-White, p. 522. Edinburgh.
Hoffman, F. L. (1934) *New Engl. J. Med.*, **210**, 507.
Huggins, C., and Hodges, C. V. (1941). *Cancer Res.*, **1**, 294.
Macalpine, J. B. (1949). *Cystoscopy and Urography*, p. 281. London.
Mulholland, S. W. (1931). *Proc. Mayo Clin.*, **6**, 734.
Registrar-General's Statistical Review for England and Wales, 1948. London.
Roth, A. A., and Turkel, H. (1944). *J. Urol.*, **51**, 66.
Wear, J. B., and Schoenenberger, A. P. (1948). Ibid., **59**, 587.

# DIAGNOSTIC VALUE OF THE GLUCOSE CONTENT OF SEROUS PLEURAL EFFUSIONS

BY

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Bacteriological confirmation of the tuberculous origin of non-purulent pleural effusions may be difficult to obtain by direct culture, while the result of a guinea-pig inoculation will not be available for several weeks. Where negative results are obtained, radiography and sputum examination may not be helpful, and a search was therefore made for other diagnostic criteria. Experience gained from glucose estimations of the cerebrospinal fluid in tuberculous meningitis directed attention to the possible diagnostic value of the glucose content of pleural fluid.

TABLE I.—*Summary of Recent Investigations*

| Author | No. of Cases | Diagnosis | Fluid Glucose Level (mg./100 ml.) | | Method |
|---|---|---|---|---|---|
| | | | Max. Value | Min. Value | |
| Foord *et al.* (1929) | 34 | Prim. tuberculous (9)<br>Sec. ,, (6)<br>Non- ,, (6) | 116<br>122<br>99 | 64<br>91<br>70 | Not stated |
| Pinner and Moerke (1930) | 32 | Tuberculous | 82 | 0 | Folin–Wu |
| Nassau (1941) | 57 | Tuberculous | 136 | 4 | Hagedorn–Jensen |
| Gelenger and Wiggers (1949) | 33 | Tuberculous (10)<br>Non-tuberculous (21)<br>,, ,, (1) | 39·5<br>140 | A trace<br>62<br>Less than 40 | Folin–Wu |
| Present series | 61 | Tuberculous (25)<br>Non-tuberculous (30)<br>"Undiagnosed" (6) | 118<br>200<br>96 | 10<br>67<br>62 | Hagedorn–Jensen |

Table I summarizes the results of four recent investigations into the glucose content of pleural effusions and includes the results of the present investigations. Foord *et al.* (1929) found that there was little variation in the glucose level of tuberculous and non-tuberculous fluids, and also that the level of the sugar in the pleural fluid paralleled the level in the blood. The method of estimating the glucose is not given, and the lack of agreement between their results and those of others may be due to the use of a method less specific for glucose than the Hagedorn–Jensen and Folin–Wu methods. Pinner and Moerke (1930) investigated only tuberculous fluids. Although they concluded that no significance could be attached to the glucose content, their results agree with those of Nassau (1941) and Gelenger and Wiggers (1949), who found the glucose content in tuberculous effusions depressed to a variable extent when compared with blood values.

Nassau used the glucose level in tuberculous pleural effusions as a prognostic aid, and stated that values over 70 mg./100 ml. were favourable and values under 50 mg./100 ml. were unfavourable prognostically. Gelenger and Wiggers in their series found that the glucose level was below 39.5 mg./100 ml. in 10 tuberculous effusions and above 60 mg./100 ml. in 21 non-tuberculous cases, and conclude that if the sugar level is above 60 mg./100 ml. it is unlikely that the effusion is tuberculous. They quote one non-tuberculous case (bronchogenic carcinoma) in which the level is below 40.

In the present series, 61 cases were examined, 25 of which were tuberculous, 30 non-tuberculous, and 6 "undiagnosed." The term "undiagnosed" is used because bacteriological confirmation of the tuberculous origin of the effusion was not forthcoming, and no other cause presented. In all the tuberculous cases the diagnosis was confirmed by bacteriological examination of either sputum or pleural fluid, or at necropsy. Of the 30 non-tuberculous cases, 13 were due to congestive heart failure, 7 to carcinoma, 1 to leukaemia, 2 followed pulmonary infarct, 1 was in association with ascites and pancreatitis, and 6 were post-pneumonic. The pleural fluid was collected two hours after the patient's last meal. In many of the cases concomitant blood sugars were taken, and these values lay within a normal range. Fluoride was used to prevent glycolysis, and the glucose was estimated by the Hagedorn–Jensen method. The results of the investigation are set out in Table II. No correlation could be found between the blood and pleural fluid glucose levels (Table III).

TABLE II.—*Results in Present Series*

| Glucose Levels (mg./100 ml.) | Tuberculous | Non-tuberculous | "Undiagnosed" |
|---|---|---|---|
| Over 100 | 4 cases | 24 cases | |
| 90–100 | 3 ,, | 3 ,, | 1 case |
| 80–90 | 1 case } 12 | 2 ,, | 1 ,, |
| 70–80 | 2 cases | | 2 cases |
| 60–70 | 2 ,, | 1 case | 2 ,, |
| 50–60 | 1 case | | |
| 40–50 | 3 cases | | |
| 30–40 | 2 ,, } 13 | | |
| 20–30 | 3 ,, | | |
| 10–20 | 4 ,, | | |
| Total No. of cases | 25 | 30 | 6 |

TABLE III.—*Blood and Pleural Fluid Glucose Levels in Tuberculous and Non-tuberculous Patients*

| Tuberculous | | | Non-tuberculous | | |
|---|---|---|---|---|---|
| No. | Pleural Fluid mg./100 ml. | Blood mg./100 ml. | No. | Pleural Fluid mg./100 ml. | Blood mg./100 ml. |
| 1 | 21 | 121 | 2 | 126 | 116 |
| 8 | 67 | 83 | 3 | 117 | 96 |
| 9 | 76 | 79 | 4 | 151 | 133 |
| 10 | 76 | 138 | 5 | 105 | 103 |
| 11 | 80 | 70 | 6 | 67 | 85 |
| 12 | 53 | 80 | 7 | 90 | 73 |
| 17 | 10 | 102 | 13 | 100 | 93 |
| 18 | 96 | 110 | 14 | 100 | 110 |
| 20 | 89 | 87 | 15 | 104 | 134 |
| 23 | 55 | 91 | 16 | 84 | 124 |
| 24 | 95 | 106 | 21 | 81 | 67 |
| | | | 22 | 132 | 120 |
| | | | 25 | 81 | 85 |

## Discussion

All 30 non-tuberculous pleural effusions had a glucose level of over 60 mg./100 ml. and in 24 of these the level was over 100 mg./100 ml. In the 25 tuberculous cases, 13 showed glucose values below 60 mg./

100 ml. Of the 12 cases above this figure, one was complicated by amyloid disease, while another was a diabetic with a glucose level in the pleural effusion of 220 mg./100 ml.

A glucose level of under 60 mg./100 ml. would therefore appear to be strongly suggestive of the tuberculous origin of a serous pleural effusion. Where the glucose level is over 100 mg./100 ml. the effusion is probably of non-tuberculous origin.

The six "undiagnosed" cases had glucose levels ranging from 62 to 96 mg./100 ml. Four of these six cases were considered clinically and radiologically to be of tuberculous post-primary type, but bacteriological confirmation was lacking. The four patients were adolescents or young adults, with straw-coloured lymphocytic effusions of recent onset, and gave positive Mantoux reactions.

There were eight tuberculous patients with glucose levels between 60 and 100 mg./100 ml. and seven non-tuberculous. The glucose values in the six "undiagnosed" cases would therefore be of no value in deciding the aetiology of the effusion.

**Summary**

The pleural glucose level has been studied in 61 cases of serous effusion.

In these cases: (*a*) a glucose level of less than 60 mg./100 ml. was found only in tuberculous effusions; (*b*) the majority of tuberculous effusions had glucose levels of less than 100 mg./100 ml., while most non-tuberculous effusions had levels above 100 mg./100 ml.; and (*c*) no significance could be attached to glucose levels of between 60 and 100 mg./100 ml.

REFERENCES

Foord, A. G., *et al.* (1929). *J. Lab. clin. Med.*, **14**, 417.
Gelenger, S. M., and Wiggers, R. F. (1949). *Dis. Chest*, **15**, 325.
Nassau, E. (1941). *Tubercle*, **22**, 249.
Pinner, M., and Moerke, G. (1930). *Amer. Rev. Tuberc.*, **22**, 121.

# ACUTE PORPHYRIA WITH UNUSUAL FEATURES

BY

**ERIKA GROSSFELD, M.B., Ch.B.**

*(From the Southern General Hospital, Glasgow)*

In view of the recent interest in this disease and its comparative rarity in this country it is thought worth while to record the following case, which presents some unusual features.

## Case Report

The patient, a woman aged 23, was admitted in December, 1949, to a surgical ward of the Southern General Hospital with a history of attacks of abdominal pain and vomiting of one week's duration. The pain usually started in the right hypochondrium and travelled forward across the epigastrium and through to the back in the upper lumbar region. It was spasmodic in nature, and severe, and an attack lasted for 15 to 30 minutes. Shortly after the onset of the pain she vomited. These attacks occurred three or four times a day. Her bowels had been regular until two days before admission, since when they had been constipated. Three days before admission her urine was red in colour on one occasion. Her menstrual history was normal, and she had just finished a period when the pain began.

There was nothing relevant in her past history except that she had had a similar attack of pain and vomiting with the passage of red-coloured urine one year previously, when she was treated for "kidney trouble" with rest in bed for six weeks at home. No further information is available about this illness.

On examination the patient was seen to be a well-grown and well-nourished woman who looked ill. She had definite guarding and tenderness in the right loin and hypochondrium but none elsewhere. Her temperature was normal, pulse 72, and respirations 16. No abnormality was detected clinically in any of the other systems. The urine was dark in colour but gave a negative reaction for both blood and bile. The test with Ehrlich's aldehyde reagent, however, was strongly positive. The importance of this was not appreciated at the time. On the fourth day a trace of bile was detected in the urine (iodine test) and a faint icteric tinge was noticed at the corners of both sclerae. The blood bilirubin then was 0.6 mg. per 100 ml., the thymol turbidity test for liver function was ++, prothrombin time 22 seconds, icteric index 4. The blood picture was normal.

In the meantime the patient's condition had not improved. The attacks of pain had persisted with almost unabated severity and were still accompanied by guarding and tenderness in the right hypochondrium. In view of this fact and the laboratory findings it was decided to perform a laparotomy with the tentative diagnosis of gall-stones. At operation, however, the biliary tract appeared perfectly normal and no other intra-abdominal abnormality was found. It was then that the diagnosis of acute porphyria was proposed. Chemical tests and spectroscopy of the urine speedily established it.

The patient had a post-operative cough and later developed pneumonia. It was noticed at that time that she had some difficulty in coughing and that her sclerae assumed a plum-coloured tinge. Temporarily she made a partial clinical recovery, but her cough persisted. On the seventh post-operative day she felt so well that she asked to be allowed to get up, and enjoyed it. She then complained of attacks of numbness in both thighs, occurring only at night and lasting for about one hour; but there was no objective evidence of peripheral neuritis, and the cerebrospinal fluid was normal. On the 14th day she first complained of weakness and could hardly raise herself in bed. The trunk muscles, thighs, and upper arms showed great loss of power, while the reflexes appeared normal. There was some improvement in the right arm and the thighs after two days, but the other affected muscles remained weak. At this time she developed tachycardia, 120 a minute, and her blood pressure rose from 108/75 to 135/95 mm. Hg. The attacks of abdominal pain had returned on the ninth post-operative day and were severe. On the 18th post-operative day she lost her voice and did not regain it. On the 24th day she had great difficulty in swallowing, and next day the diaphragm became involved and she died with a generalized flaccid paralysis.

During the whole course of her illness the urine was pigmented, the intensity varying from a faint pink tinge to a deep port-wine colour.

*Further Investigations.*—Once the diagnosis of acute porphyria was established a number of other investigations were carried out in an attempt to find out to what extent the different systems were involved in the disease. The liver function tests carried out on the 19th post-operative day were as follows. Plasma proteins: total, 8.12 g.% (albumin 3.88 g., globulin 4.24 g.). Laevulose-tolerance test: fasting 2.4 mg., half-hour 8 mg., one hour 13.1 mg. per 100 ml. Thymol turbidity test ++; cephalin-flocculation test negative; van den Bergh test negative, direct; blood bilirubin, 1.35 mg. per 100 ml.; icteric index, 6.

Bile could not be detected in the urine post-operatively. On the 12th post-operative day the serum chloride and sodium levels were 325 mg.–336 mg. per 100 ml. respectively. Renal-function tests were carried out from the 12th to the 18th post-operative day and showed no abnormality: urea-clearance test 82%; urea-concentration test, concentrated to 4.6 g.% in the second hour; blood urea, 26 mg. per 100 ml. The blood picture on the ninth post-operative

day was: red cells, 5,840,000 per c.mm.; Hb, 14 g.%; P.C.V., 52%; M.C.V., 89 $\mu^3$; M.C.H.C., 27%; white cells, 10,000 per c.mm. The water-excretion test (Kepler–Power) was carried out on the 24th post-operative day and gave the following results: largest volume of day urine, 21 ml.; volume of night urine, 72 ml.; urine urea, 3.4 g.%; urine chlorides, 320 mg./100 ml.; plasma sodium chloride, 565 mg./100 ml.; plasma urea, 45 mg./100 ml.; value of "A," 33. The urine contained 285 mg. of uroporphyrin per litre at the time of death.

*Post-mortem Examination.*—The lungs showed mucopus in the larger bronchi and patches of unresolved pneumonia at both bases. No abnormality was detected macroscopically in any of the other systems. Sections of the lungs showed bronchopneumonia Sections of the brain and spinal cord showed none of the characteristic features of the disease.

*Family History.*—The mother died, aged 49 years, of a "stroke," the father in his seventies with "dropsy." Three brothers and two sisters are well; their urines were examined, and none contained porphyrins. Two cousins on the mother's side died young—one at 23 years, diagnosed as from acute ascending myelitis, the other at 21 years, diagnosed as from anxiety neurosis and pneumonia.

### Discussion

Porphyria is a disease believed to be due to an inborn error of metabolism which results in the circulation of an excess of porphyrins in the blood. It has been suggested that porphyrins exert a toxic action, particularly on nervous tissue (Mason, Courville, and Ziskind, 1933; Vannotti, 1937; Thorner, 1937). The condition was first described as a clinical entity by Günther (1911). Since then a number of cases have been reported, particularly in Scandinavian and American literature, and the condition has been excellently reviewed by Nesbitt (1944). In this country attention has been drawn to the disease only recently (Chandler, Harrison, and Rimington, 1939; Discombe and D'Silva, 1945; Jörgensen and With, 1947; Abrahams, Gavey, and Maclagan, 1947; Discombe, 1948; Petrie, 1948; Davies, 1949; Gibson, Harrison, and Montgomery, 1950; Hart and Collard, 1950).

This case presents a number of the usual features of the disease. The patient had abdominal pain, neurological manifestations, tachycardia, and arterial hypertension, and she passed pigmented urine. But the most interesting and confusing feature was the marked guarding and tenderness in the right hypochondrium; this is a feature which has not been reported before, and was very largely responsible for the delay in arriving at the correct diagnosis. Her family history is also interesting, as the stories of the fatal illnesses of her two cousins suggest that they, too, may have suffered from acute porphyria.

The serum chloride and sodium levels were estimated and the Kepler-Power test was carried out because it has been suggested that there is some adrenal insufficiency in this disease (Abrahams, Gavey, and Maclagan, 1947). This contention cannot be supported by the present case. The lowering of the serum chloride and serum sodium has also been attributed to impaired renal function rather than adrenal disturbances (Davies, 1949), but again in this case we could find no evidence of renal disorder. Since this patient's serum sodium and chloride values showed no significant deviation from normal we cannot expect to throw light on this particular problem, but it is evident from this case that lowering of sodium and chloride concentration in the serum is not an invariable accompaniment of the disease.

Various drugs such as sulphonal, methylsulphonal, barbiturates, lead, etc., have been incriminated in the production of this disease. This patient stated that she did not take any drugs before her admission.

My thanks are due to Mr. W. A. Mackey for his advice and encouragement, to Dr. J. W. Chambers and Dr. A. Dick for carrying out the biochemical and pathological investigations, and to Professor Rimington for doing the estimation of porphyrin.

### References

Abrahams, A., Gavey, C. J., and Maclagan, N. F. (1947). *British Medical Journal*, **2**, 327.
Chandler, F. G., Harrison, G. A., and Rimington, C. (1939). Ibid., **2**, 1173.
Davies, D. (1949). Ibid., **1**, 846.
Discombe, G (1948). Ibid., **2**, 659.
—— and D'Silva, J. L. (1945). Ibid., **2**, 491.
Gibson, Q. H., Harrison, D. C., and Montgomery, D. A. D. (1950). Ibid., **1**, 275.
Günther, H. (1911). *Dtsch. Arch. klin. Med.*, **105**, 89.
Hart, F. D., and Collard, P. (1950). *British Medical Journal*, **1**, 278.
Jörgensen, J., and With, T. K. (1947). *Lancet*, **1**, 54.
Mason, V. R., Courville, C., and Ziskind, E. (1933). *Medicine*, **12**, 355.
Nesbitt, S. (1944). *J. Amer. med. Ass.*, **124**, 286.
Petrie, E. (1948). *British Medical Journal*, **1**, 926.
Thorner, M. W. (1937). *J Amer. med. Ass.*, **108**, 969.
Vannotti, A. (1937). *Porphyrine und Porphyrinkrankheiten*, p. 286. Springer, Berlin.

# Medical Memoranda

## Failure of Aureomycin in Dermatitis Herpetiformis

Conflicting reports of the value of "aureomycin" have been published recently. In America Robinson *et al.* (1949) treated five cases of dermatitis herpetiformis with from 1 to 2 g. of the antibiotic daily. They reported invariable relief from itching and involution of vesicles within one to two weeks, and that the response was more rapid and satisfactory than could be expected with any previously known treatment. Clarence Shaw (1950) used aureomycin in two patients suffering from dermatitis herpetiformis and reported complete failure to influence the course of the disease in either patient. The dosage he used was 1 g. daily for two weeks.

Recently I have had the opportunity of treating a severe case of dermatitis herpetiformis with this drug.

### Case Report

A married woman aged 68 developed erythema of both forearms in May, 1950. By July the lesions had become vesicular, involving the forearms and backs of hands, and spreading rapidly to the legs, thighs, buttocks, face, and neck, with groups of vesicles and bullae scattered over the chest and back, and accompanied by considerable itching. At no time were the mucous membranes affected.

Before admission she had received a course of penicillin injections (2,500,000 units in a week), then a course of sulphadimidine (32 g. in four days), and, finally, sulphapyridine 1 g. four times daily for a week (total, 28 g.). No improvement was noted with these measures, vesicles and bullae continued to form, and she was admitted to hospital.

*Investigations.*—Bulla fluid contained "a few leucocytes—no eosinophils." The patch test (potassium iodide, 20% in soft paraffin) was strongly positive. Nikolsky's sign could not be elicited. Blood eosinophilia varied between 13% and 34%. Biopsy report: "A subepidermal bulla, in the floor and lumen of which are numerous eosinophils. There is no evidence of pemphigus. Diagnosis—dermatitis herpetiformis."

Aureomycin capsules were administered orally in dosage of 250 mg. four times daily for seven days, and then increased to 500 mg. for a further two weeks. In all, a total of 35 g. was given in three weeks. At no time was there any objective or subjective improvement in the condition. The bullae continued to form (some as large as a walnut) and became increasingly widespread. No toxic side-effects were noted apart from a feeling of warmth and excessive sweating.

Aureomycin was considered to have been valueless in this case, and was discontinued. The patient was then given liquor arsenicalis, 10 min. (0.6 ml.) four times daily, and within a week her general condition had improved, the erythema lessened, and no further vesicles formed. She was discharged from hospital two weeks later with the disease apparently controlled by the arsenic.

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REFERENCES

Robinson, H. M., Robinson, H. M., jun., and Robinson, R. C. V. (1949). *J. invest. Derm.*, **13**, 9.
Shaw, C. (1950). Ibid., **14**, 3.

## Cholelithiasis in a Boy of 10 Presenting as Acute Appendicitis

The following case is of interest because of the comparative rarity of such a condition in children, and because it presented as an apparently classical case of acute appendicitis.

### Case Report

The patient, a boy aged 10, was admitted to hospital on September 5, 1949, at 8.45 a.m. At 11 p.m. the previous night he had complained of the sudden onset of peri-umbilical pain; this had persisted overnight, getting worse at times and then better. Early on the morning of admission it had shifted to the right iliac fossa, where it remained, of fairly severe intensity and sharp in character. Shortly after the onset of abdominal pain he had vomited up his tea and supper, and this had made the pain worse. His bowels had not moved since the onset of pain. There was no dysuria or frequency. He had had a similar but less severe attack four days before admission, lasting only an hour or so. There was nothing relevant in his previous history. His mother said that he had always been a very healthy youngster.

On examination his general condition was fairly good. His skin was a good colour, and there was neither pallor nor flushing of his cheeks. His temperature was 98.4° F. (36.9° C.) and his pulse 96. The abdomen was not moving very freely on respiration, and there was guarding over and also tenderness in the right iliac fossa. Rövsing's sign was positive. Nothing abnormal was found in the cardiovascular, respiratory, and central nervous systems.

A diagnosis of acute appendicitis was made, and the child was taken to the theatre for laparotomy at 2 p.m. on the day of admission.

*Operation.*—The abdomen was opened through a right lower paramedian incision, and the appendix was found in the ileo-caecal angle; it was about 4 in. (10 cm.) in length and the seat of a mucocele, but not of any actual infection. In view of the negative findings in the appendix, the mesentery was examined carefully for any sign of acute non-specific mesenteric adenitis. However, only a few glands were found, some partially and some completely calcified, presumably from an old tuberculous infection.

Palpation higher up on the right side of the abdomen revealed a greatly distended transverse colon and a sausage-shaped mass below the edge of the liver. The original incision was lengthened at this point to give easier access to the liver and gall-bladder region. The gall-bladder was found to be grossly distended and inflamed; it was two to three times its normal size, and a stone was palpated in Hartmann's pouch. In view of the great distension of the transverse colon and the relative smallness of the patient, it was decided not to attempt to remove the gall-bladder. The stone was milked back into the fundus of the gall-bladder, a purse-string suture inserted, and a small incision made over the stone, which was then delivered. The purse-string suture was tightened and tied. A corrugated-rubber drain was inserted under the right costal margin and brought out through a stab incision in the right flank. The abdomen was closed in layers.

*Pathological Report on the Gall-stone.*—Macroscopic examination revealed a tar-coloured waxy stone ½ in. (1.25 cm.) in diameter, containing a nucleus of brown material of somewhat softer consistence. It was a mixed stone, composed mainly of cholesterol, with traces of bile pigment, calcium, phosphates, and fatty material.

Post-operative progress was good. The patient was given a course of sulphadiazine over five days, and this settled a slight pyrexia. The drain was removed on the ninth post-operative day. He was discharged on September 22 feeling very well indeed.

### Comment

While the comparative rarity of cholelithiasis and cholecystitis in children in itself gives interest to this case, the complete absence of symptoms and signs referable to gall-bladder disease is of even more interest.

Ladd and Gross in *The Abdominal Surgery of Childhood* state that only about 450 cases of gall-bladder disease in children are recorded in the literature. They find that cholelithiasis is commoner than acute cholecystitis, and say that the stones tend to remain in the gall-bladder. The commonest symptoms are right upper quadrant pain, nausea, vomiting, and fever. The commonest cause of gall-stone formation in children is said to be haemolytic anaemia. This case showed no evidence of such an aetiology.

I should like to thank Mr. Douglas G. Martin, surgeon-superintendent, St. Richard's Hospital, Chichester, for permission to publish this case.

PEARL A. WALKER, M.B., Ch.B.,
Lately House-surgeon, St. Richard's Hospital, Chichester.

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The Principal of the University of London (*Report for the Year 1950–1*) refers to the impact of the National Health Service Act on the facilities for medical education, which continues to create problems. Following on last year's dispute with the Ministry of Health over the function and remuneration of registrars in the London teaching hospitals, which was finally settled to the satisfaction of the University, the Ministry issued in November its well-known circular suggesting drastic reductions in the numbers of registrars. However, the problems involved are receiving further consideration, and the Ministry appears to be ready to compromise, though nothing has as yet been settled. The Ministry has now amended the Appointment of Specialists Regulations in a way which for the most part meets the objections raised by the universities. Concerning clinical posts, where the salaries are paid out of university funds, each university is now free to make its own arrangements with the teaching hospital concerned. In addition universities have been allowed four representatives out of eight on the appointment boards which make recommendations about filling posts on the staffs of teaching hospitals. For the first time since 1933 the undergraduate medical schools of the University of London were visited on behalf of the Senate by inspectors; they drew attention to a number of serious deficiencies, the most important being the shortage of clinical facilities in the teaching hospitals. A report of their findings and the recommendations made has been sent to the Ministry.

# Reviews

## JUVENILE DELINQUENCY

*Unraveling Juvenile Delinquency.* By Professor Sheldon Glueck and Dr. E. T. Glueck. (Pp. 399. £2.) New York: The Commonwealth Fund. London: Geoffrey Cumberlege. 1950.

Dr. and Mrs. Glueck are well known for their studies of the American criminal. Hitherto their investigations have been concerned chiefly with the efficacy of different modes of treatment; this has now led them to attempt an analogous inquiry into the problem of causation. Different schools of psychiatry, as they point out, are apt to subscribe to very different causal theories, and each "too often insists that the truth is to be found only in its own special field." They themselves decided to adopt the procedure which was first applied to criminological problems in Britain—namely, making intensive case studies of two matched groups of delinquents and non-delinquents respectively, and applying a rigorous statistical analysis to determine which causal factors are genuinely significant. Accordingly they selected 500 offenders from the city of Boston, nearly all between 5 and 14 years, and paired each with a non-delinquent of the same age, sex, intelligence, neighbourhood, and race. By means of tests, questionaries, and other devices, a systematic inquiry was then undertaken into the health, physical type, intelligence, temperament, character, and home background of each one.

Their conclusions may be summed up as follows. Physically delinquents belong, with few exceptions, to what W. H. Sheldon has called the mesomorphic type: that is, they exhibit a physique in which there is a relative predominance of muscle and bone. This, it is considered, points to the influence of innate or genetic factors. Intellectually they tend to express themselves through direct and concrete activities rather than by the use of abstract processes, such as reasoning or reflection; their mean intelligence quotient is only 92. In temperament they exhibit a marked degree of emotional instability, and are of an extraverted rather than an introverted type. Their parents tend to be inferior in almost every respect—physically, intellectually, emotionally, and morally. Delinquency itself is thus nearly always the outcome, not of any single pathological trait, but of a plurality of converging factors. It will be seen that these several conclusions agree to a remarkable extent with those already reached by British psychologists who carried out similar investigations in London and elsewhere.

One feature of special interest is that the plan of the investigation enables the writers to eliminate certain causal factors frequently cited by previous writers. They find, for example, that feelings of inferiority and of insecurity are actually less common among delinquents than among non-delinquents. Emotional stress, as reported by the psychiatrist on the basis of interviews, was not found to be specially characteristic of the delinquent group. "Although it is often assumed that many delinquents are psychopathic, only 36 of the 500 are thus characterized; and neuroticism is more markedly present among the non-delinquents." Indeed, both in physical and in mental health the delinquents differed scarcely at all from the control group. Detailed tables of the findings are given in appendices; and, on the basis of their statistical calculations, the authors claim that, by using similar methods of psychological and social assessment, it should be possible to predict, at or soon after the age of entering school, which children are most likely to drift into delinquent habits, and so to substitute preventive methods for curative. The whole research has been admirably planned and carried out, and forms a model of its kind.

CYRIL BURT.

## CATARACT

*Surgery of Cataract.* By Daniel B. Kirby, A.M., M.D., LL.D. (Pp. 695; 339 illustrations, including 52 subjects on 21 colour plates. £12.) Philadelphia and London: J. B. Lippincott Company. 1950.

Daniel B. Kirby, of New York, has established an international reputation as one of the foremost exponents of the techniques of cataract surgery, and it is to be expected that a monograph from his pen on a subject he has made a life's study would be valuable and informative. Those who know Kirby personally would also expect it to be unusual. All these expectations are fulfilled. The author's attitude is clearly reflected in his writing; he lives for the surgery of cataract, and each individual operation is a drama in which the surgeon is author, producer, and star. The theatre must be worthy, grey-tiled, and air-conditioned, its illumination perfect in its minutiae, and the drapes grey-green; the instruments must be perfect in their style, weight, and balance; the assistants and nurses must be minutely trained and rehearsed in their various parts; and the surgeon, his correct behaviour, his psychology, and his mode of life are fully outlined. He must dedicate himself to his work, eschewing alcohol, nicotine, and caffein; he must ensure that by diet and supplement to diet he receives the proper supply of vitamins and minerals.

As an introduction to this picture the author describes the development of the surgery of cataract from its early emergence in the Hindu, Chinese, and Graeco-Egyptian cultures. He discusses the basic principles of the anatomy and physiology of the lens; and he describes in detail, with a wealth of illustrations, the various types of pathological opacification in this tissue, developmental and acquired by disease or trauma. Medical treatment for cataract is dismissed as ineffective, and the historical development of the many operations for dealing with the various types of cataract and the details of each technique are discussed with great thoroughness. Not the least interesting features are the advice given on the preparation of the patient, the original contributions the author has himself made to the subject, and the discussion of the post-operative complications which may arise, with guidance on how these may be circumvented or treated. Where it is possible—the indications and contraindications are fully and fairly given—the author favours early removal of the lens by the intracapsular method and has a preference for three radially placed post-incisional sutures.

The book is excellent, unusual in its detail, complete in the presentation of the opinions of others as well as the author's own, lavishly illustrated, and beautifully produced.

STEWART DUKE-ELDER.

## TROPICAL MEDICINE

*Diseases of the Tropics.* By George C. Shattuck, M.D. (Pp. 803; 131 figures. $10.) New York: Appleton-Century-Crofts, Inc. 1951.

In his preface the author of this book states that the primary objective in its preparation was to offer at moderate cost a concise but comprehensive account of the diseases of the Tropics. He presents the subject matter in 12 separate parts of varying length, arranged in no very obvious pattern. A curious omission is that of the enteric group of fevers, especially as epidemic and endemic typhus occupy a chapter of reasonable length. Admittedly the former are not peculiar to the Tropics, but they are none the less very common there and are so important in the differential diagnosis of the many obscure fevers which occur in warm countries that their absence leaves an important gap. Apart from this the scope of the work is comprehensive. The layout within the different sections is logical, the descriptions are lucid, the illustrations are excellent, and the lists of references are useful, though few are later than 1948. There seems indeed to have been considerable delay in publication, for, although the date given is 1951, the newer antibiotics receive no more than passing mention, and other recent work, such as the treatment of leprosy with the parent sulphone, diamino diphenyl sulphone, is missed altogether.

In general the teaching is sound, though it is obvious, and indeed inevitable, that the author has little, if any, first-hand experience of some of the subjects on which he writes. This results in a certain lack of perspective which detracts from the practical value of the book. To quote a single instance: the subject of suppression of malaria receives much less attention than it deserves. Data concerning the suppressive action of the different antimalarial drugs are mixed up with those on therapy, and there is no balanced account of the advantages and disadvantages of each compound in this role to serve as a guide to the tyro. On the other hand, rather more than a page is devoted to the diagnosis of "latent" malaria by sternal, spleen, and liver puncture.

The subject of tropical medicine has now expanded to such an extent that it is beyond the capacity of any one person to write a comprehensive and up-to-date textbook. Only an edited symposium with chapters on each subject written by experts is likely to be satisfactory. However, no modern book of this type exists, and in its absence the volume under review will no doubt prove of value to many.

J. S. K. BOYD.

## TREATMENT OF TYPHOID CARRIERS

*Typhoid and Paratyphoid B Carriers and their Treatment.* Experiences from Western Norway. By Th. M. Vogelsang, M.D. (Pp. 368. No price.) Bergen, Norway: A. S. John Griegs Boktrykkeri. 1950.

The campaign against typhoid and paratyphoid B in Western Norway, started by the late Dr. Magnus Haaland at Dr. Gade's Institute in Bergen a few years after its establishment in 1912, has been systematically pursued by his successor, Professor Th. M. Vogelsang. He has paid special attention to chronic carriers of these diseases, and now reviews his work in this monograph, which is in English. It is dedicated to the memory of his former chief, Dr. Magnus Haaland, and appears as the first of a medical series of publications which the newly created University of Bergen will issue from time to time.

In the opening pages the author discusses the history of the subject and the contributions made to it by other observers, but most of the book is on the prodigious work carried out so perseveringly at Dr. Gade's Institute over many years. Professor Vogelsang paints a very tragic picture of the lot of the typhoid carrier, however conscientiously she is dealt with by the medical authorities. She is often an old woman whose fate it is to be hunted from pillar to post, disowned and shunned by her relations and friends, treated by the authorities as more dangerous than a leper. Little wonder therefore that she gladly accepts such a drastic measure as the removal of her gall-bladder in some instances. Professor Vogelsang's review of the less radical methods is as discouraging as his record of operative treatment is hopeful. His material consists of 75 carriers of *S. typhi* and 55 carriers of *S. paratyphi-B*. Seventy-eight were discovered as the result of a systematic search for the source of infection, and 38 were convalescent carriers. Nearly all were faecal carriers, but there were four who were apparently only urinary carriers. In a few cases both faeces and urine were infected. As many as 58 carriers were operated on, cholecystectomy being performed in all but two of these cases. Four-fifths of those undergoing cholecystectomy were free from their infection. Professor Vogelsang's indications for this treatment include the demonstration of the specific organism in the bile by means of the duodenal tube and of the presence of gall-stones or functional disturbances of the gall-bladder. But we have to face his admission that, "Whether the interval between infection and operation be long or short, a certain number of carriers will continue to discharge the specific germ after cholecystectomy."

C. LILLINGSTON.

## BOOKS RECEIVED

*Review is not precluded by notice here of books recently received*

***How To Look At Illness.*** By N. Glas, M.D., L.R.C.P., M.R.C.S. (Pp. 48. 3s.) London: New Knowledge Books. 1951.

***The Hell Bomb.*** By W. L. Laurence. (Pp. 198. 9s. 6d.) London: Hollis and Carter. 1951.

***Latex Technique and its Application to Chiropody.*** By F. A. Drew, F.Ch.S. (Pp. 44. 3s. 6d.) London: The Actinic Press. 1951.

***The Transactions of the Hunterian Society 1949-50.*** Vol. 8. (Pp. 133. No price.) London: Hunterian Society. 1951.

***Clinical Uses of Intravenous Procaine.*** By D. J. Graubard, M.D., and M. C. Peterson, M.D. (Pp. 84. 8s. 6d.) Oxford: Blackwell Scientific Publications. 1951.

***The Trials of Patrick Carraher.*** Edited by G. Blake. Notable British Trials Series. Vol. 74. (Pp. 278. 15s.) London: William Hodge. 1951

***Microscopic Staining Techniques No. 3.*** Edited by E. Gurr, F.R.I.C., F.R.M.S., F.L.S. (Pp. 64. 3s. 6d.) London: Edward Gurr. 1951.

***Symposium on Diseases of the Skin*** and ***Symposium in Honor of William Sharp McCann.*** Nationwide Number of the Medical Clinics of North America. (Pp. 329. No price.) London: W. B. Saunders. 1951.

***Memorias do Instituto Oswaldo Cruz.*** Vol. 48. (Pp. 732. No price.) Rio de Janeiro: Servico Grafico do Instituto Brasileiro de Geografia e Estatistica. 1950.

***Abdominal Distension and Intestinal Activity Following Laparotomy.*** By A. Höyer. (Pp. 207. Kr. 15.) Oslo: Nationaltrykkeriet. 1950.

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## WORLD MEDICAL ASSOCIATION

The Annual General Assembly of the World Medical Association will be held in Stockholm in September of this year, when Dr. Dag Knutson, who is assistant physician at the Karolinska Hospital and president of the Swedish Medical Association, will take over the presidency from Dr. Elmer L. Henderson. It is expected that about 200 delegates and alternate delegates will be present at the meeting. The delegates will assemble in the second chamber of the Riksdag, the Swedish Parliament. Meetings of the Council of the W.M.A. will immediately precede and follow the Assembly. In the first week of May the Council of the W.M.A. met in Geneva to receive the reports of the various committees which have been at work on their respective problems since the October meeting of the W.M.A. in New York last year.

At Geneva senior officers of the W.M.A. held a series of important conferences with representatives of W.H.O. (World Health Organization) and with I.L.O. (International Labour Office). The relationship between W.M.A. and these special agencies of the United Nations has been of some concern to W.M.A. since it was established in 1946. It was felt to be especially desirable that the respective fields of work of W.M.A. and W.H.O. should be clearly defined so that these two international organizations, having the same broad aims in common, should be able to reach these with the minimum of misunderstanding and conflict. Some overlap of fields of work is inevitable. With a clear understanding of each other's immediate objects this overlap should be lessened, if only for the sake of avoiding duplication of work. But in some cases, as, for example, medical education, it is hoped that the combined activity of W.M.A., W.H.O., and other bodies will be of undoubted benefit. The Secretary-General of W.M.A., Dr. Louis H. Bauer, in his oral report to the W.M.A. Council, was able to show that the discussions held with W.H.O. had done much to clear the air. It is, of course, necessary to emphasize that the W.M.A. represents, at an international level, the physicians and surgeons who are the members of national medical associations—represents, that is to say, some half-million doctors in most of the non-Communist countries. W.H.O., as a special agency of U.N., is an inter-governmental organization, and therefore fundamentally represents the views of the health departments of its member States. It is obvious, therefore, that in some respects the approach to certain problems will differ, even sharply, as between the W.M.A. and the W.H.O. Nevertheless, there is a wide area of common interest, and an important first step has been taken to bring the two organizations together on those matters that make co-operation possible. Anything which can lessen mutual suspicions is to the good.

During the eight days in Geneva last month the committees of Council and the Council itself worked long hours in carrying their various projects a stage further, so that they will be in a position to give an account of their stewardship at the meeting of the General Assembly in Stockholm in September. In the regrettable absence through ill-health of the Chairman of the Council, Dr. T. C. Routley, of Canada, the proceedings were most ably conducted by the Vice-Chairman, Dr. P. Glorieux, of Belgium. As on previous occasions, social security was much to the fore in the minds of members of Council. In so far as schemes for social security affect the medical profession—as they must do—it was plain that this is of intense interest to those national medical associations represented in W.M.A. The committee on social security has collected many facts on medicine in relation to social security, and is considering an ambitious scheme for collecting and collating still more facts so that these may be available for those interested. In a report from this committee, the chairman of which is Dr. Knutson, it was pointed out that anything in a medical service under a social security scheme which lessened the patient's sense of responsibility heavily increased that of the doctor, and that where the citizen was given increasing rights to this and that benefit he tended to think more of his rights than of his duties.

Once more the Council had before it the controversy between the International Office of Documentation of Military Medicine and the W.M.A. about a professional code of ethics. As is well known, the W.M.A. has put down in the Declaration of Geneva and the International Code of Medical Ethics a set of rules for professional behaviour which has been widely acclaimed. For an international association of military doctors to try to lay down, as it has done, such a code for all doctors is an intervention which the W.M.A. has strongly resisted. The W.M.A.'s action on behalf of doctors in civilian practice deserves widespread recognition.

What perhaps roused most interest at the Council meeting in Geneva was the report by Dr. J. A.

Pridham, chairman of the committee on medical education. In October last year it was suggested that the W.M.A. should sponsor an international conference on this subject of perennial importance to the medical profession of all countries, and perhaps never more so than at the present time. In Dr. Pridham's report it was thought that such a conference should attempt to find answers to the following questions: (1) What is the aim of undergraduate medical education? (2) What should be the requirements for entry into medical studies? (3) What should be the general character of the curriculum after entry? It will be necessary to make thorough preparation for such a conference, and in this the W.M.A. will seek the collaboration of other interested bodies—collaboration in financing as well as in planning the conference, which, if all goes well, may be held in London. In addition to receiving reports from other committees, the Council had before it the April issue of the *World Medical Association Bulletin*, edited by Dr. Morris Fishbein. Among many other interesting items there is an account in this issue of the Fourth General Assembly at New York last year. The *Bulletin* is in English, French, and Spanish, and thus affords a useful opportunity for English readers to brush up their knowledge of the other two languages.

It is perhaps difficult for the individual member of the B.M.A.—or of any other national medical association—to grasp the significance of W.M.A. to himself or herself. Time, distance, and money make it possible for only a relatively few to attend the annual general assembly. Yet it is important for medical men and women to know that the W.M.A., by the nature of its organization, has very much at heart the impact upon the individual practising doctor of all those matters that affect his professional and social life. In these days, when Governments are more and more providing publicly the personal services of doctors to their patients, the vigilance of such an international body as the W.M.A. is more than ever necessary. Not only that, but the interchange of information between doctors from different parts of the world is something which cannot fail to be of benefit, especially to those countries in need of help and information about all sides of professional life. The W.M.A. is gathering strength and confidence, and it is encouraging to note that it is determined to tackle, at an international level, medical education. This is the root of the matter of medicine. Unless the principles and practice of medical education are on a sound foundation the doctor will not be able to apply in his practice the judgment and skill needed to give his patients all that modern medicine has to offer.

## METHONIUM COMPOUNDS IN HYPERTENSION

The assessment of the value of any new treatment in hypertension is extremely difficult, for blood pressure often settles with rest and reassurance, and symptoms may clear with little change in blood-pressure level. Opinion on the value and place of potassium thiocyanate, of thoraco-lumbar splanchnicectomy, and of the rice diet in the control of high blood pressure is still divided, though the progress of the disease has certainly been modified in many cases. The introduction of the long-acting ganglion-blocking drugs, the salts of pentamethonium and hexamethonium, led to the hope that the medical interruption of vasomotor tone might also prove of value in the treatment of hypertension. Since the original paper by Paton and Zaimis,[1] these compounds have been widely used; many would say too widely, for they are undoubtedly potentially dangerous drugs that should be given only under carefully controlled conditions.

The drugs were first administered by intravenous or intramuscular injection,[2] and it was found that in normotensive subjects, while there was little change of blood pressure in the supine position, marked hypotension occurred on standing up. In the hypertensive patient a marked fall of blood pressure occurred while supine, and an even greater fall followed the assumption of upright posture. It was soon found that these drugs could be given by mouth, though much larger doses were required to produce the same effect on blood pressure. It is probable that the high ratio between the effective oral and parenteral dose is due to failure of absorption, and studies on the excretion of the compounds in the urine[3] support this view. The variability of response to oral dosage and the reported occurrence of severe hypotensive or other toxic effects may be related to sudden increased absorption.

A series of authors[4-6] have reported favourably on the control of blood pressure by oral administration, though certain difficulties have arisen. The uncertainty of absorption has already been mentioned; acquired tolerance to oral dosage is frequent and the dose may have to be much increased, and even then it may cease to be effective; and, finally, toxic effects from the large dose of the associated anion, bromide, have been reported. The observed hypotensive action

1 *Nature, Lond.*, 1948, **162**, 810.
2 Arnold, P., and Rosenheim, M. L., *Lancet*, 1949, **2**, 321.
3 Milne, G. E., and Oleesky, S., *ibid.*, 1951, **1**, 889.
4 Turner, R., *ibid.*, 1950, **2**, 353.
5 Saville, S., *ibid.*, 1950, **2**, 358.
6 Campbell, A., and Robertson, E., *British Medical Journal*, 1950, **2**, 804.
7 *Ibid.*, 1951, **1**, 778.
8 *Ibid.*, 1949, **1**, 791.
9 Restall, P. A., and Smirk, F. H., *N.Z. med. J.*, 1950, **49**, 206.
10 Smirk, F. H., *ibid.*, 1950, **49**, 637.

cannot, however, be ascribed to the bromide ion, for other salts have proved equally effective. Locket and his colleagues[7] have recently reported a series of cases treated orally by these drugs and concluded that they were hardly more effective in lowering blood pressure than bed-rest alone. While their paper confirms the importance of controlled observations, it is doubtful whether their condemnation of the drugs is fully justified. They make no mention of the measurement of blood pressure in the upright posture, and their figures, being the average of readings over two-day periods, give no clear picture of the effectiveness of the single dose.

Last year Professor Smirk[8] outlined the view that hypertension resulted from many causes and that the higher the level the more severe the secondary effects and the greater the chance of the hypertension being perpetuated or increased. If this view is accepted, the lowering of the blood pressure during the major part of the day, and while in the upright posture, might be expected to be of considerable advantage. Elsewhere in this issue Smirk and Alstad extend the original reports from New Zealand[9 10] on the use of the drugs by subcutaneous injection. This route has the advantage of more prolonged action than intravenous or intramuscular injection, while the dosage is far less than is needed orally, and tolerance, though often increased after a short period of treatment, is less complete and can be countered by increased dosage. Their results and conclusions are as optimistic as Locket's were pessimistic, and their method is clearly an advance in harnessing these potent drugs for clinical use. Both objective and subjective improvement is recorded in the majority of their patients, and the value of the drugs is confirmed in such complications of hypertension as papilloedema, retinitis, pulmonary oedema, and headache. There would appear to be some measure of agreement that the cautious use of pentamethonium or hexamethonium salts in these complications is of great value. The special interest of their paper, however, lies in their account of 32 patients treated for over six and up to fourteen months. The patients gave themselves the injections, just as the diabetic gives himself insulin. Their results are impressive. In view of the difficulties of oral administration, the subcutaneous route is now being widely tried. Smirk and Alstad experienced no serious complications in their large series of cases, but these must clearly be expected when a potent drug is being tried out in a dangerous disease; complications (and even death) have been reported in orally treated cases, so that the subcutaneous route must be used with great caution.

The drugs have been mainly used in cases of essential hypertension, but they have also proved effective in some patients with renal hypertension and with toxaemia of pregnancy. They may be of value in certain cases of chronic nephritis complicated by hypertension, but, in the presence of renal failure, must be used with great care, since excretion may be delayed and action prolonged. Caution must also be exercised in treating patients with evidence of cerebral or coronary arterial disease, for the sudden lowering of blood pressure may lead to relative local ischaemia and possibly to thrombosis.

Many of the new and potent drugs that have been introduced of recent years require very careful supervision, and often the control of therapy depends upon laboratory findings. The effective use of the methonium compounds demands the very careful personal supervision of each patient. The effect of small doses must be followed over a period of hours. Treatment is then started with small doses, the blood pressure being recorded at frequent intervals, and the dose gradually increased as tolerance occurs until a maintenance dose is reached. This may require alteration from week to week. Smirk[10] has already published full details of his procedure.

Time will show whether these new drugs represent as definite an advance in the long-term control of hypertension as they do in the treatment of complications, and whether the ultimate prognosis of the disease is improved. At the present time there seems no justification for their widespread and uncontrolled use in mild benign essential hypertension. Until the method of use, the dosage, and the expected effects are more clearly defined, the treatment should be reserved for carefully selected and controlled cases who can be closely observed during the early weeks of treatment.

## CHILDREN IN NEED

The break-up of the Poor Law and its replacement, in so far as the neglected child is concerned, by the new machinery of the Children Act of 1948 has brought about many improvements in the last three years. Children's committees have striven towards the ideals of the Curtis report in creating, among much else new, children's homes and reception centres; and the Central Council for Training in Child Care has sought to provide trained staff. For these reasons the recently published report[1] on the work of the Children's Department of the Home Office is of exceptional interest. Out of about 55,000 children in the care of local authorities, approximately 19,000 are boarded out with foster parents and

30,000 are in children's homes. There are a further 29,000 in the care of voluntary organizations (of whom 25,000 are in children's homes and 3,500 are with foster parents), and 35,000 children boarded out by their parents and supervised through child-life protection schemes (25,500 in independent schools, 7,500 in private foster homes). Thus about 120,000 children are supervised by children's committees. The percentage of children who are boarded out by these committees has risen slightly since 1946—from 29 to 35%. The small home of not more than 12 children (usually in an ordinary house in an ordinary street), so strongly advocated by the Curtis Committee, has made a little progress, with only 41 new units opened. The grouped homes, consisting of groups of cottages holding 10 to 20 children in the care of a house-mother—a less preferable method, because "it creates in the aggregate a large community of children in care who are too numerous to be absorbed readily in the ordinary life of the neighbourhood"—does not appear to have been extended. The ideal of the small family unit either in group or scattered homes is not very much nearer, and, partly because of building difficulties, students leaving training courses are often disappointed to find themselves at work in barrack-like institutions of the old Poor Law type.

Adoption, the fostering of children for gain, boarding out, children's homes, residential nurseries—both short-stay and long-stay—remand homes, and approved schools are all products of family disintegration. The children needing care may be illegitimate, destitute and abandoned, taken to "care and protection" either by the local authority acting on its own initiative or at the order of magistrates, delinquents, children whose parents pay others to care for them, and children who need to be removed temporarily owing to illness or other adverse circumstances at home. The integration of these diverse arrangements under the children's officer has been a wise step, but the separation of the work from the health department of the local authority is a great disadvantage. Community health can be achieved only upon the basis of the happy family; both environmental and personal hygiene have this at heart, and most of the services of the health department are therefore concerned ultimately with this one object. It is in this respect that many experienced medical officers of health consider that the Children Act has failed most signally. The Home Office report emphasizes the "overlapping and division of effort among different Government departments and different committees of the local authorities" which existed before the Act came into operation, and by inference it suggests that unity has now been achieved. In fact, the disunity is as great to-day as it was before the Act, for the real unification must be of the means of attack on the social conditions which lead to children being deprived of a normal home life, and the work done under the Children Act needs to be reintegrated with all the other measures that are taken to safeguard community health. It would be a logical step to place the children's officer, whose work for the individual child can be invaluable, on the staff of the medical officer of health. The disadvantages which can arise from the separation of the work of the children department from that of the health department can be seen clearly in connexion with health visiting. Children's departments employ separate boarding-out visitors to supervise boarded-out and foster children. In theory these visitors are supposed to be able to pay more attention to the educational aspects of child development than health visitors could, but in fact this special visitation underlines the difference from its fellows of the unfortunate child who has lost its own home at a time when this is the last thing to be desired. The visiting of children in foster homes, boarded-out children, the selection of suitable homes, and the visiting and examination of adopted children and those placed with a view to adoption would best be done by the ordinary staff of the health department under the immediate direction of the children's officer.

The disunity which the Children Act has produced within the field of social medicine has affected the official approach to the "problem family." The Home Office report has a chapter on the subject of children neglected or ill-treated in their own homes. This gives the impression that the solution of the problem family, if indeed one can be found, lies within the ambit of the children's officer and the children's committee. How far this impression has already gone can be seen from the action taken under the joint circular[2] issued last summer by the Home Office, Ministry of Health, and Ministry of Education: this was addressed to county and county borough councils and asked for an officer to be designated who could be responsible for the co-ordination of the work relating to the child neglected in its own home. The report states that "about half of the officers designated so far are children officers; most of the others are clerks of councils or medical officers of health, while some authorities have selected the chief education officer." This increased interest in the child neglected in its own home, which has arisen from public agitation leading to a debate in Parliament, is in fact a pointer to the steady growth of appreciation of the importance of prevention. A child

[1] Sixth Report of the Work of the Children's Department of the Home Office, 1951, H.M.S.O., London.
[2] Joint Circular of the Ministry of Health (78/50), Home Office (157/50), and Ministry of Education (225/50), dated July 31, 1950.

neglected away from its home has at one time been a child neglected in its own home. One estimate of the number of children in problem families is 300,000 compared with the total of 55,255 children in the care of local authorities at the end of 1949. Many disorders of community health, delinquency included, often originate from neglect of children in their own homes. Ascertainment must be early and will usually be done by the health visitor, often in collaboration with the general practitioner. If the family is to be lifted out of the " problem " category, all the resources of the health department must be used—the sanitary inspector, the school medical officer, the home nurse, the home help, the mental health social worker, and, of course, the health visitor. Whatever the administrative implications of the joint circular, this is work of the first importance for all health departments.

## REMUNERATION OF GENERAL PRACTITIONERS

The General Medical Services Committee held a special meeting on May 24 to receive a report from its representatives of their discussions with the Minister of Health on the remuneration of general practitioners. A brief statement of this appears in this week's *Supplement*. In addition, the Committee had before it a letter from the Minister, the proposals of which were considered to be unsatisfactory. The G.M.S. Committee met on Thursday of this week, and at the time of going to press we are unable to say whether or not it has received from the Minister a reply to a letter which was sent to him at the end of last week. It was considered inadvisable at this stage to make public the contents of the Minister's letter. There are, however, some facts in the situation which need to be emphasized. Of these, the most outstanding is the Spens report on the remuneration of general practitioners—a report which is now some five years old and therefore in danger of being temporarily lost sight of.

The essence of the Spens report was that it laid down, in the 1939 terms of money, a standard of living for general practitioners, and it recommended that there should be a varying distribution of income for practitioners of different ages and responsibilities. In view of the importance of general practitioners in any medical service, the idea behind the recommendations of the Spens Committee was that it should provide a financial return which would continue to attract able men and women. The Spens Committee was concerned that the recruitment and status of general practitioners should be maintained as against other professions, and its financial proposals were directed towards this end. During the past three years there have been endless discussions on relating the Spens proposals to the present-day value of money, a correction which the Spens report—accepted by both the Government and the profession—said should be made. Yet it still appears to be difficult to get exact figures on which such a necessary adjustment can be made, or to get agreement on what the adjustment should be. It is the absence of these facts and this decision that makes general practitioners feel frustrated and disgruntled, and it is surely in the interests of everybody that the prolonged period of delay and prevarication should come to an end.

It is essential in this situation to hold fast to the basis laid down by the Spens report. Its acceptance by the Government, for example, makes it clear that the central pool must be enlarged to keep pace with the increase in the number of general practitioners, when there is such an increase. The Spens report did not lay down that such-and-such a sum of money should be available centrally, but that certain proportions of general practitioners should receive certain ranges of income, to be adjusted according to the change in the value of money. The Ministry of Health, in arriving at its initial figure for the central pool, aimed at a sum which, with its own betterment factor (not accepted by the profession), would satisfy the requirements of the Spens Committee. If ever the size of the central pool were to be divorced from the Spens recommendations, then general practitioners would be at the mercy of any arbitrary decision made by a Minister of Health, introduced for whatever apparently sound reason. To-day, for example, we are faced with the decision of the Government (supported by the Opposition in Parliament) that there should be a ceiling of £400m. for the National Health Service. Such a ceiling has become necessary because of the lack of economic foresight of Mr. Aneurin Bevan in planning the Health Service. His successor has had the misfortune to inherit this legacy of extravagance. As a result, general practitioners now find themselves in the highly invidious position of being at the bottom of the queue.

The present Minister of Health, Mr. Hilary Marquand, has shown his sympathy with the position of the practitioners in the N.H.S. and has admitted that there is a case for reviewing their remuneration. The trouble is that this case has so often become obscured by irrelevancies. Fundamentally, the matter is simple. The medical profession wants to know whether or not the Spens recommendations are now being met in terms of the current value of money. It surely is time that the facts were laid openly upon the table to enable those concerned to decide whether or not this is so.

## NEONATAL JAUNDICE AND ANTIBODIES

The syndrome of icterus gravis neonatorum, resulting from iso-immunization against Rh, is well known. A similar condition, in which iso-immunization against the A or B factor is a possible cause, has also occasionally been reported. Physiological jaundice, on the other hand, occurs in nearly 50% of newborn infants and is most marked when birth is premature; it is usually ascribed to functional immaturity of the liver, an idea supported by the experiments of Mollison.[1] However, the similarity in broad clinical outline between physiological jaundice and icterus gravis has caused several workers to consider whether the former might also be a mild result of iso-immunization against blood-group factors. Wiener, elsewhere in this issue, examining a small sample, finds no correlation between physiological icterus and incompatibility of ABO or Rh factors, which seems to diminish the possibility, though other known blood groups should be similarly investigated and the possible influence of groups yet unknown also considered.

The problem might be approached by trying to demonstrate sensitizing antibodies in the mother or foetus. Aidin, Corner, and Tovey[2] described a neonatal condition of jaundice, kernicterus, and prematurity in which no antibodies were detected and the direct antiglobulin test was negative. Wiener postulates, however, that the responsibility may lie with maternal "cold auto-antibodies" which are universally present and capable of crossing the placenta and attaching themselves to the foetal red cells. The activity of these "cold antibodies" may be facilitated at birth by the precipitate entry of the infant into an environment colder than that of the uterus. A similar hypothesis was invoked by a Spanish author to account for neonatal icterus in mules.[3]

The interest of this suggestion lies in the consideration of what can properly be regarded as an antibody; this matter is also discussed by Wiener.[4] In the present state of our knowledge it is doubtful whether it is wise to accord to "univalent cold auto-agglutinins" the full status of antibodies. They do not seem to enjoy in any marked degree certain features commonly associated with immune antibodies—namely, specificity, firmness of combination, and origin from the known stimulus of a foreign antigen—yet they can mimic some of the serological reactions by which antibodies are recognized *in vitro*. They may be detected by agglutination, by lysis under special conditions,[5] by the anti-globulin test,[6] and by using trypsinated red cells; though the last technique is inherently prone to be non-specific. The situation recalls the uncertainties of specificity which beset the serology of syphilis. To apply the term antibodies to those substances which simulate immune reactions *in vitro* may be no worse than imprecision, but, in the absence of experimental proof, to assume that their presence may invoke such dynamic consequences as haemolysis *in vivo* is more dangerous.

1 *Lancet*, 1948, **1**, 513.
2 Ibid., 1950, **1**, 1153.
3 Cited by Puget, E., *Rev. méd. Vet., Lyons et Toulouse*, 1948, **99**, 503.
4 *J. Immunol.*, 1951, **66**, 287.
5 Dacie, J. V., *J. Path. Bact.*, 1950, **62**, 241.
6 —— *Nature, Lond.*, 1950, **166**, 36.

## DELINQUENT BOYS

We publish this week on another page a summary of the report[1] of the Joint Committee on Psychiatry and the Law appointed by the British Medical Association and the Magistrates' Association to consider delinquency in adolescent boys. The size of the problem can be judged from the figures published by the Home Office in *Criminal Statistics*. In 1938 there were 19,387 boys between the ages of 12 and 17 found guilty of indictable offences. In 1948 the number had increased to 27,545. The report seeks to examine the special characteristics found more frequently among delinquents of these ages, and emphasizes the wide variety of the causes that appear to be at work. It lays most stress on home circumstances. No precise figures are given, but the committee found that a large number of delinquent boys are members of households that are neglected, overcrowded, and even criminal; many come from families where the parents are divorced or where matrimonial disharmony exists; and some are adopted children. The report concludes, and the conclusion will be readily accepted by all who have had experience in this field of work, that personal relations are far more important to the child than material circumstances. Other influences, such as that of the cinema, street companions, dance halls, and the temptation to gamble on horses, dogs, and football pools, are discussed in turn; and the war, it is argued, must have operated as a major factor, not merely by increasing the disruption of family life, but also by aggravating the problem of housing. The results of intelligence tests appear to show that many delinquents are below average in innate capacity; and many, it is said, have suffered from inadequate schooling. Above all, adolescents are particularly prone to go through a phase of emotional instability and impulsiveness; and their inclination is nearly always to seek jobs yielding immediate high wages which very often turn out to be blind-alleys.

The committee makes a number of practical recommendations: education authorities should modify the curriculum during the last year of school life so that neither the pupils nor their parents should feel that this additional year is wasted; sex education and sex guidance should be instituted; there should be far greater co-operation between parents and youth organizations; special attention should be given to appropriate placing in industry, particularly of the dull and backward; and, finally, further research on the problem should be undertaken without delay.

Dr. Lucien Bovet,[2] of Lausanne, reached similar conclusions in a contribution to the United Nations "Programme for the Prevention of Crime." After summarizing the many investigations carried out during recent years in various countries on the causes and treatment of delinquency at all ages, he, too, insists first and foremost on the fact of multiple causation. Psychiatric writers, he finds, still express very contradictory views: some attribute delinquency almost wholly to innate constitution, others to environmental and social conditions; very few

1 *The Adolescent Delinquent Boy*, 1951. Published by the British Medical Association. Price 3d.
2 *Psychiatric Aspects of Delinquency*, 1951, World Health Organization, Geneva.

have recognized that in nearly every instance both types of factor are at work. Until the end of adolescence pathological conditions, whether physical or mental, are of little influence. "A large proportion show no major physical or psychological abnormality: they are simply the victims of adverse external circumstances; and, in general, organic disease is not of overwhelming importance in the aetiology of antisocial behaviour: before puberty true psychosis plays almost no part, nor are the fully fledged neuroses of much importance." Emotional instability, on the other hand, is extremely common. Dr. Bovet himself believes that most cases have a threefold origin—biological, psychological, and social. Treatment must be adapted to each individual delinquent, and should be "based on the fundamental laws of psychology." In view of the wide differences of opinion that still obtain, more research and more publicity are needed. In Dr. Bovet's opinion this should lead to better facilities and more appropriate training courses for those who will be directly concerned with the problem of delinquency.

## RESPIRATORY TUBERCULOSIS IN SCOTLAND AND ENGLAND

In Scotland the trend of pulmonary tuberculosis in the last 12 years has differed from the trend in England and Wales. In 1939 the death rate in England and Wales was 52 per 100,000 of the population; it rose to 59 in 1940, to 60 in 1941, declined to the pre-war level by 1944, and then continued to fall, being 44 in 1948, 40 in 1949, and 32 (provisional figure) in 1950. This is a notable decline and seems to be continuing this year; in the first 20 weeks of 1951 the number of deaths in the great towns from tuberculosis was 3,712, a reduction of about 10% on last year's comparable figure of 4,138. In Scotland the death rate from respiratory tuberculosis was 54 per 100,000 in 1939; it rose to 62 in 1940, reached 66 in 1947 and 1948, fell to 60 in 1949, and fell again to 47 in 1950. In England and Wales no marked changes occurred in the mortality in different age groups during this period, but in Scotland changes of this kind were recorded. For several years before the war the greatest mortality among females in Scotland was in the age group 15–24, but the rise in mortality was most marked at ages 25–34, so that this age group became as important as the younger one. In 1938 the death rates per 100,000 were 101 for ages 15–24 and 74 for ages 25–34: these rates had increased to 142 and 147 respectively by 1947, and to 150 and 149 respectively in 1948. A small rise from 45 in 1938 to 56 in 1948 was recorded for ages 35–44, but for other age groups over 45 the death rates in 1948 were slightly below those of 1938. The age of maximum mortality also shifted for the males, though the increase was not so impressive as in the case of the females. The male mortality per 100,000 in 1938 for the age groups 25–34, 35–44, 45–54, and 55–64 were 83, 85, 98, and 79 respectively, while in 1948 the rates were 99, 96, 119, and 129. For the first three age groups the trend of the death rates has been irregular, and each had a maximum value during 1938 and 1948, but at ages 55–64 a continuous rise has been recorded in the death rates since 1940. Thus it would appear that the reduction of mortality from respiratory tuberculosis presents a different problem in males and females. Tuberculosis in young adults is to a large extent the result of recently acquired infection, while much of the disease in later life is probably due to latent infections flaring up or to a second infection. While various hypotheses to explain the different age distribution of mortality between the sexes can be advanced, a satisfactory assessment of the different influences which may play an important part—for instance, physiological, biological, and socio-economic factors—is not practical.

The difference in the trend of respiratory tuberculosis in Scotland and in England and Wales during recent years is not easily explained. It has been suggested that the facilities for isolation and treatment are better in England and Wales than in Scotland, and consequently the tendency for a rise in mortality was counteracted earlier in England and Wales than in Scotland. It is very unlikely that this is the only factor, since the number of notifications has steadily risen in all three countries, and all have experienced a serious shortage of sanatorium beds. In England and Wales 37,879 cases of respiratory tuberculosis were notified in 1938, and this number gradually increased to 43,971 in 1949. In Scotland 4,657 cases were notified in 1939, and a continuous rise occurred in the following years until 1949, when 8,653 cases were notified, but in 1950 a small decline to 8,138 cases was recorded. The introduction of mass radiography probably accounts for some of the initial increase, but the continuous rise is unlikely to have been due solely to this, even if many of the new cases were only insignificant lesions that formerly would have escaped attention altogether. It seems probable that there has been a real increase in incidence, but a puzzling feature in the figures for England and Wales is the decline in the death rates if the incidence has really increased, especially since there has been an acute shortage of sanatorium beds.

## NEW HOSPITAL FOR TROPICAL DISEASES

With the opening of a spacious new building in St. Pancras, the London Hospital for Tropical Diseases, which was founded by Sir Patrick Manson just over half a century ago, enters upon a new era. The building, in St. Pancras Way, adjacent to the former L.C.C. hospital of St. Pancras, was built in 1939 and was intended as a maternity wing, but it has now been adapted and equipped in the most modern manner to serve the purpose of tropical medicine. It accommodates 68 in-patients, which is 20 more than at the premises in Devonshire Street which the hospital has just vacated.

Manson's original hospital was at the Albert Dock, located there for convenience in treating seamen, and it served as a centre for the study of tropical disease. The hospital remained in dockland until after the first world war, and then, with the School of Tropical Medicine attached to it, it was removed to Endsleigh Gardens in Bloomsbury, where there were 77 beds. In 1924 the

school joined forces with the London School of Hygiene, established by the University of London, thanks to the generosity of the Rockefeller Foundation, in the fine building in Keppel Street, but functionally the school and the hospital continued as one unit. At the beginning of the second world war the hospital was closed and later was severely damaged by a land mine, but as soon as the war was over a large nursing-home in Devonshire Street was taken and equipped as a hospital of 48 beds.

At St. Pancras it is hoped to carry on in better and roomier quarters the clinical researches which have for so many years distinguished the hospital and the school. The move will enable the London School of Hygiene and Tropical Medicine to introduce a longer course of eight months, which will include four continuous months at the hospital. It will make it easier for hospitality to be offered to medical men from home or overseas who wish to devote their attention to this specialty, and it is hoped to bring about a wider interchange of doctors, students, and nurses with hospitals and schools abroad. The hospital will be the yellow-fever inoculation centre for south-east England, and a mobile vaccination team will visit the London docks to inoculate ships' crews making only a few hours' stay. The new hospital, which is only a mile or so from the London School of Hygiene and Tropical Medicine, was opened by the Duchess of Kent on Empire Day. It is one of the University College group of hospitals.

## CLOTHING WANTED

On page 1266 of this issue there is a letter from the Ladies' Guild of the Royal Medical Benevolent Fund appealing for clothes. Readers will be well acquainted with the R.M.B.F. Christmas appeal, but what is not so widely realized is that clothes of all kinds (especially children's and large sizes) are always wanted for the many beneficiaries of the Guild. Parcels are sent out twice a year to dependants of members of the medical profession who need help, most of all children of school age and old people; the plea for warm nightclothes and underwear is never ending. The Guild appeals to all those with clothes to dispose of, however few, to remember them.

In addition the Guild provides many other most valuable services. As well as making grants for the training and maintenance of children, help is given towards school fees, uniforms, lunches, and holidays. Where there is great need gifts in kind are often made to replace broken furniture, and so on. A small number of grants are made for domestic help—greatly appreciated by the elderly and frail—also a small number for convalescence. A scheme to lend wireless sets was made possible by a legacy from a former beneficiary, but this is now almost entirely used up. Cheques are sent in winter to those who would otherwise be unable to buy coal; last year £357 was devoted to this fund. There are at present 142 branches of the Guild in Britain, and new members and subscribers are always most warmly welcomed.

## AND SO TO BURLINGTON HOUSE

In the early days of the Royal Society it used to be one of Robert Hooke's duties to devise a new experiment each week for demonstration to the assembled Fellows on Friday evening. Nearly three centuries have passed since then, science has become infinitely complicated and scientists devilishly sophisticated, and all that remains of the Society's custom of staging displays of natural phenomena is an annual evening party at Burlington House, the Conversazione. This year there were about 30 demonstrations, mostly fairly elaborate in style though basically straightforward in conception, with their inventors at hand to explain in simple language what was going on. Several were concerned with the sea. One showed how samples can be bored from the deep-sea floor and analysed to reveal the history of the earth's climate over a million years. Another was a special camera which took a series of flashlight photographs of the sea bottom 150 ft. down—a kind of marine census. There were tanks with living hermit crabs in transparent shells, delicate pink and greenish shrimps staring up with black bulbous eyes, long feathery worms swimming gently in coils, and an octopus asleep. And in a great transparent slowly turning wheel full of sea water swam a tiny "jellyfish" (medusa): an apparatus for measuring the speed of swimming and changes induced by the alternation of an artificial day and night. There were skulls of South African ape-men with ridged brows and massive jaws and carious teeth, dead a million years ago; and dinosaur skin impressions in stone from the Upper Cretaceous. Films were shown on snakes and their bites (in colour) and on the harmless freezing of spermatozoa and red cells to −79° C. in the presence of glycerol. Many of the other exhibits conformed to the original purpose of the Society to study "such knowledge as hath a tendency to use."

It is rare, even in London, to see science dynamically displayed with living animals and apparatus in action on the frontiers of research, but the Conversazione is only for the Fellows and their guests. It seems a pity that the demonstrations cannot afterwards be transferred each year for exhibition to the general public, at the Science Museum or elsewhere. Or, better still, they could form a travelling show, spending a week or a fortnight in each of the principal provincial museums. If the Ministry of Education cannot sponsor it, the British Association for the Advancement of Science could well do so; the problems of transport, staffing, and finance are not great. Such a show would stimulate enthusiasm in schools, would be useful propaganda for science among a wide public, and could well be entertainment bearing the same relationship to the peep-show and the fairground as the zoo has to a circus.

There is a continual risk that science should seem too remote and theoretical, but public experiments—as in Pepys's day—can do much to show it to be real, tangible, and practical, as it was at this year's Conversazione.

# *REFRESHER COURSE FOR GENERAL PRACTITIONERS*

# TREATMENT OF SQUINT IN CHILDREN

BY

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Although in the treatment of certain disorders of function of the human body it may be expedient to adopt a "wait and see" or expectant policy in the hope that the condition will right itself with the passage of time, such a policy should not be adopted in the treatment of squint in children, an exception being made only in the case of an infrequent intermittent squint lasting but a few seconds, which is sometimes encountered in young infants when teething. Many cases of squint are rendered unnecessarily difficult to treat because they have been neglected in the early stages.

Squint is apt to be regarded purely as a physical deformity. People are inclined to forget that a squint results in the loss of an important physiological function—namely, that of binocular vision. When a squint is present the visual axes of the two eyes are not pointing in the same direction, hence the two eyes cannot be used together to obtain binocular vision, and as a result there is loss of the ability to appreciate perspective.

One would naturally expect that, if the eyes were looking in different directions, diplopia would result, as indeed it invariably does in the case of an adult who, having previously possessed normal binocular vision, has acquired a squint as a result of an ocular palsy due to disease or injury. In the case, however, of a young child whose binocular functions are as yet not fully developed, diplopia is at the most only a fleeting symptom. Mental suppression of the image formed in the squinting eye rapidly takes place. This usually gives rise to a definite loss of vision in the squinting eye (amblyopia), unless the squint alternates from one eye to the other. Amblyopia, if allowed to develop, may require prolonged occlusion of the non-squinting eye before it is overcome.

It should be realized by all who are responsible for giving advice to parents about a child's squint that once a permanent squint has become established it will not disappear without adequate treatment. The fact that in some cases of (untreated) unilateral convergent squint a gradual reduction of the angle of deviation may occur, rendering the eyes cosmetically straight by about 40 to 50 years of age, albeit without the function of binocular vision, and possibly with one relatively blind eye, is no excuse for not treating the condition adequately in infancy.

## Diagnosis

Unless a squint is diagnosed in the early stages it is idle to talk about the importance of its early treatment.

Although a squint of large degree, especially a convergent squint, is obvious to any casual observer, one of small degree, and none the less important for that, may easily be overlooked. A squint of not more than 10 or 12 degrees may be undetectable by mere inspection, and may necessitate refined methods of examination for its diagnosis. On the other hand, one must bear in mind the possibility of the existence of an apparent squint. The illustration shows a case of pseudo-convergent strabismus, in which it was thought that a squint was present, but the squinting appearance

Pseudo-convergent-strabismus due to broad epicanthic folds.

was due to the presence of broad epicanthic folds. These made the eyes appear to be "closely set" when the gaze was directed forwards and made the adducting eye appear to turn in excessively when the gaze was directed to one side.

A squint of sudden onset is naturally easier to detect than one of more gradual onset, especially if the latter is only slowly progressive. At its onset a squint may be variable and intermittent, or it may occur only in certain directions of the gaze and for certain distances of fixation. Precise information about the mode of onset, the exact anomaly observed, its variability and duration, and other details given by an intelligent observer are of the utmost importance. A squint of the intermittent type may not be "obliging" at the time of examination, but if there is a clear-cut history of such a condition given by a reliable observer the diagnosis is unlikely to be in doubt.

It is also desirable to inquire into the family history, for in a doubtful case of squint a strong family history of the condition makes one more suspicious.

The simplest test for the presence of a squint is as follows.

Make the child fix his gaze on a spot-light (in the case of a young infant it is advantageous to keep the light flashing on and off in order to attract attention), then, while watching the right eye, quickly occlude the left eye: if the right eye exhibits a movement in order to take up fixation of the light as soon as the left eye is covered, it follows that it must have been squinting before the left eye was covered. The direction of such a movement of the right eye will give evidence of the direction of the squint—for example, if the right eye turns outwards to take up fixation it must have been in a convergent position before the left eye was occluded, and therefore there is a right convergent squint. There will be a precisely opposite observation in a divergent squint and comparable observations in vertical squints. If, on the other hand, the right eye remains fixing the light, there is no manifest squint of the right eye.

A similar procedure is then carried out, covering the right eye and observing the left eye. The test should be repeated at least twice to ensure correct observation. Furthermore, the test should be carried out if possible using a distant fixation light as well as a near one, for sometimes a squint may exist when the gaze is directed in the distance and not when it is directed towards a near object or vice versa.

As a result of this "cover test" it will be clear whether there is (*a*) a manifest squint of the right eye, (*b*) a manifest squint of the left eye, (*c*) an alternating squint of either eye: it will also determine the type of deviation and whether the squint is present both for near and for distant fixation or only for one or the other; or (*d*) no manifest squint of either eye, in which case the test may demonstrate the presence of a latent squint—that is, a deviation of the occluded eye due to dissociation, with recovery of binocular fixation when the occluder is removed.

Although this test can be easily carried out by anyone not fully versed in ophthalmology, the following difficulties may be experienced: (1) the squinting eye may be so defective in vision (amblyopic) that it does not fix readily, or it may fix eccentrically; (2) the angle of deviation may be so small that the movement of the eyes is difficult to detect; and (3) the child may be too young and/or too inattentive to keep his gaze fixed on the light.

Apart from deciding whether a squint is present or not, it is important to determine, if possible, the state of the vision in each eye. If the child is not old enough for his vision to be tested by means of Snellen's test types, or by the illiterate "E" test, or by picture test types, then some idea of the visual acuity may be obtained by investigating, by means of the cover test, the capacity of the child to fix with each eye.

The ocular movements should be examined in all directions of the gaze to determine if there is any limitation of movement, which may be suggestive of an ocular palsy, or if there is any excessive movement, which may be suggestive of overaction or contracture of a muscle. The pupils and their reactions should also be examined, and the eyeballs as a whole, both externally and ophthalmoscopically.

Before discussing the line of treatment to be recommended in any case of squint, let us consider why a squint develops in a child.

## Convergent Squint

### Paresis or Paralysis

In some cases a child is born with a paresis or paralysis of one or more of the extrinsic ocular muscles. If this is so there is usually an obvious squint, either in all directions of the gaze or only in certain directions (depending upon the extent of the palsy) noticeable within the first year of life. One would of course expect the squint to be noticeable from birth, and indeed it may be, but in view of the fact that ocular motility is not fully exercised until the maculae are properly developed at about the age of 6 months the squint may pass unnoticed until after this age. This is especially true of those cases in which the squint is manifest only in certain directions of the gaze, binocular vision being retained in other positions of the gaze. In some of these cases the squint is more or less overcome by the adoption of a compensatory head posture.

A paralytic or paretic squint may also occur as an acquired condition due to a febrile illness—for example, measles. Surgical treatment is invariably required in cases of squint of paralytic origin.

### Refractive Errors

*Hypermetropia.*—Although all infants are hypermetropic to a greater or less extent, on account of the relative shortness of the infant eyeball, in some cases the hypermetropia is excessive. This may lead to over-accommodation in order to obtain clear vision. Over-accommodation tends to lead to over-convergence (since accommodation and convergence are synergic actions), and this may precipitate a convergent squint. Furthermore, even in the absence of excessive hypermetropia a squint of the "accommodational" type may occur owing to an incoordination of the functions of accommodation and convergence. In these cases the squint usually begins in an intermittent fashion and tends to start, as one would expect, at the age at which the eyes are beginning to be used for discriminating near objects—usually at about 2½ to 3 years.

*Congenital Myopia.*—An infant born with a moderate degree of myopia may develop a convergent squint because he can only see clearly objects which are situated at close range. As all distant objects appear blurred there is no incentive for the child to straighten his eyes when looking in the distance.

*Anisometropia and Other Dissociating Factors.*—Gross difference in the refraction of the two eyes may be a predisposing cause of squint because it produces images of unequal size and clarity on the two retinae. This tends to make fusion difficult and may cause dissociation. In a similar way an artificially produced anisometropia, such as may be caused by the wearing of incorrect glasses, may precipitate a squint. Prolonged occlusion of one eye by temporarily dissociating the two eyes may also cause a squint to develop.

In general a child with a squint caused by a refractive error essentially needs that error to be corrected by means of a pair of glasses, although other treatment may also be needed.

### Other Causes

These include psychological factors—for example, sudden shock—familial factors, and conditions which may lead to general lowering of resistance—for example, excessive fatigue or general ill-health, especially if a latent squint already exists. Although these factors should be dealt with, their removal may not of necessity have any effect on the squint.

Secondary convergent squint may occur owing to loss of vision in the squinting eye due to organic ocular disease.

## Divergent Squint

*Primary.*—By far the largest number of cases of divergent squint begin in an intermittent fashion at the age of 3 to 5 years, or sometimes later, and appear to be due to some form of inherent neuromuscular incoordination. If untreated the squint tends to become more frequent and of larger degree and eventually it may become a constant squint. There are three main types: (1) those of the *divergence excess* type, in which the squint occurs when the patient is looking into the distance; (2) those of the *convergence insufficiency* type, in which the squint occurs when the patient is looking at a near object; and (3) those of a mixed type. Although orthoptic treatment may lessen the "attacks" of squint and considerably improve the condition, surgical treatment is usually needed to effect a cure.

*Refractive Errors.*—Uncorrected unilateral myopic astigmatism may be the underlying cause of unilateral divergent strabismus affecting the myopic eye. Uncorrected *bilateral* myopia manifesting itself in later childhood may cause divergent strabismus, usually of

the alternating type. This type of squint, however, is rarely encountered nowadays, although it was not uncommon in the days before the routine examination of the eyes of schoolchildren was carried out. The essential treatment in these cases is correction of the refractive error.

*Paresis or Paralysis.*—Weakness of the medial rectus, which may be due to a partial third nerve palsy, may be the cause of a divergent squint.

*Secondary divergent strabismus* may occur as a result of loss of vision due to organic ocular disease in the eye which is diverging.

### Vertical Squint

In practically every case of vertical strabismus there is a paretic or paralytic cause involving one or more of the vertically acting muscles. It must be remembered that pure vertical strabismus is a rarity. It usually occurs in association with convergent or divergent strabismus, and for its cure operative treatment is usually indicated.

### Treatment

Although from the foregoing description it might be thought that every case of squint can be fitted into a water-tight aetiological compartment, this is untrue, for in many cases of squint there are several aetiological factors present.

The full function of binocular vision is not developed until about the age of 3 years, the elaboration of this function and its further development continues until about the age of 5, and the complete "grounding" of the binocular reflexes is not achieved until about the age of 8. Thus in the early years of life a squint may be precipitated by some trivial obstacle, even if it acts only temporarily, as in the covering of one eye for a few days on account of an injury of, say, the eyelid—an obstacle which in the case of an adult with well-developed binocular reflexes would not have the slightest effect. Just as the bonds which unite the eyes physiologically may be rapidly broken, so, *provided that immediate treatment is given* to restore parallelism of the visual axes, they may be quickly reunited. But if the squint is left untreated, then the eyes tend to develop along dissociated lines and prolonged re-educative treatment may be needed to restore normality of physiological function, to say nothing of precise surgical treatment to restore normality of anatomy.

The eyes should first be examined under the full cyclop'egic action of atropine (atropine drops or ointment of 1% strength should be used for both eyes twice daily for three days before the examination). The reasons for this examination under cycloplegic and mydriatic are (*a*) to examine the optic fundi and media and to exclude the possibility of a "secondary" squint—that is, a squint secondary to organic ocular disease; and (*b*) to determine the state of refraction and to prescribe glasses to correct relevant refractive errors.

Naturally, if an organic ocular lesion is found the treatment resolves itself into that of the cause. The prognosis then depends on the nature and site of the lesion. An operation may be required sooner or later if only on purely cosmetic grounds. Although this group of cases forms but a small percentage of the total cases of squint in children, the possibility of a squint being due to organic ocular disease or to disease of the central nervous system must be born in mind constantly.

In the cases with refractive errors it is clearly useless to prescribe glasses unless they are going to be of some benefit. They may be of benefit because they overcome the squint, reduce the angle of deviation, or improve the visual acuity. It is a mistake, however, to adopt a complacent attitude towards a case once glasses have been prescribed, and the limitation of their benefit must be fully understood. Unless the wearing of glasses causes the squint to disappear and the eyes to function normally together (binocularly) at least half of the time, and this within a few days of wearing the glasses (this can be ascertained only by refined methods of examination), then it may be assumed that other treatment will be needed, and needed immediately. This, first of all, consists in occlusion of the normally fixing eye. Occlusion should be continued until the vision of each eye is equal as determined by testing with Snellen's test types or the illiterate "E" test, or by the picture test. (If the child is not old enough for these tests the occlusion should be continued until free alternation occurs.) In some cases atropine drops instilled into the usually fixing eye may be used for occlusion to make the child "use" the squinting eye. Atropine is, however, quite useless unless it reverses the squint.

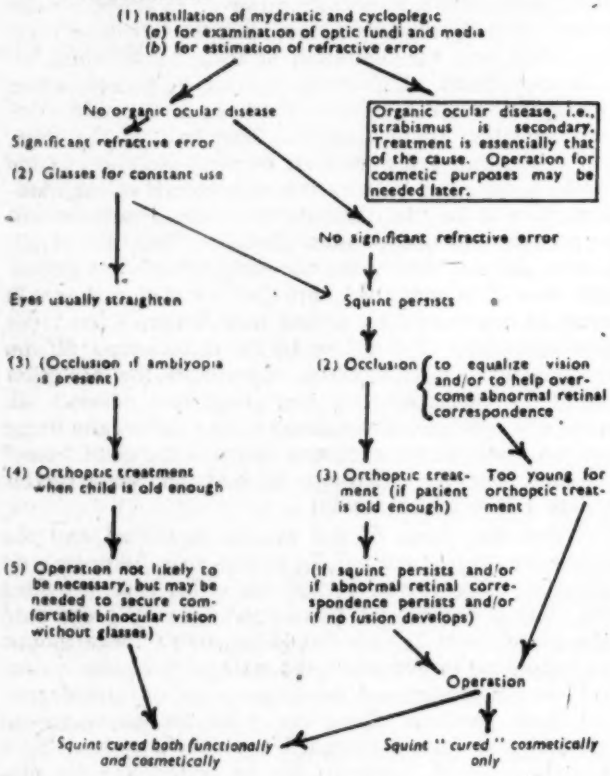
When the vision of the eyes is equalized and the refractive error corrected the squint may disappear; on the other hand it may persist. In either case, provided the child is old enough to co-operate (usually not until the age of about 3), tests should be carried out (orthoptic examination) to determine the state of binocular vision. If *fusion* is present and the squint is not of large degree, orthoptic exercises alone (or with the assistance of glasses) may restore normal binocular functions. Such exercises should, however, not be undertaken for prolonged periods unless definite progress is being made. On the other hand, if the child is not old enough or if the squint is of large degree, *operation* should be carried out at once. If abnormal retinal correspondence is present orthoptic treatment may be able to overcome it and to restore normal binocular functions, although unless there are signs of this taking place after about two months it is wiser to proceed with surgical treatment, for once the visual axes of the two eyes are restored to parallelism there is always a reasonable chance, provided there is equality of vision, of spontaneous development of normal physiological functions. (It should be stressed that operative treatment often has to be performed in a series of stages and it should be persevered with until the eyes are straight in all circumstances.)

There is a small percentage of cases in which, in spite of occlusion and the absence of ophthalmoscopic abnormality, improvement of vision in the squinting eye does not occur. In these cases there is probably a congenital retinal lesion, or a lesion due to traumatic retinal haemorrhage at birth. Treatment consists in an operation for cosmetic purposes in early childhood.

In view of what has already been said about the development of the binocular reflexes it should be pointed out that if a squint starts at a very early age—for example, within the first few months of life—there is no need to operate immediately, but it is wise to do so before the age of 18 months to 2 years in order to give the child a reasonable chance of developing normal binocular vision.

The accompanying schematic summary gives the method of treatment recommended in any given case of strabismus.

*Outline of Treatment for a Child with a Squint (Excluding Rare Cases Associated with Obvious Disease of the Central Nervous System)*


(1) Instillation of mydriatic and cycloplegic
(a) for examination of optic fundi and media
(b) for estimation of refractive error
No organic ocular disease
Significant refractive error
(2) Glasses for constant use
Organic ocular disease, i.e., strabismus is secondary. Treatment is essentially that of the cause. Operation for cosmetic purposes may be needed later.
No significant refractive error
Eyes usually straighten
Squint persists
(3) (Occlusion if amblyopia is present)
(2) Occlusion to equalize vision and/or to help overcome abnormal retinal correspondence
(4) Orthoptic treatment when child is old enough
(3) Orthoptic treatment (if patient is old enough)
Too young for orthoptic treatment
(5) Operation not likely to be necessary, but may be needed to secure comfortable binocular vision without glasses)
(If squint persists and/or if abnormal retinal correspondence persists and/or if no fusion develops)
Operation
Squint cured both functionally and cosmetically
Squint "cured" cosmetically only

## Conclusion

It cannot be overstressed that the treatment of squint may be a prolonged and painstaking business. It entails careful preliminary examination and frequent visits to check progress. The surgical treatment of squint is not just one wave of the surgical wand. It may entail operative treatment in several stages. The restoration of comfortable binocular vision does not of necessity follow as a result of wearing correct glasses or of surgical intervention. Prolonged occlusion to equalize the vision of the two eyes and orthoptic re-educational exercises may be required. But—and this is the important point—if a squint is treated energetically and efficiently directly it begins, the prognosis is usually good, and, even if it is not possible in all cases to restore binocular single vision, it is possible in most cases to ensure that the child will grow up in possession of two useful seeing eyes, and, indeed, what is just as important, will grow up without the psychological disadvantage of being "cross-eyed."

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The Ministry of Health is drawing attention to certain possible changes in prescribing. Hospital quality cotton-wool, which has the same absorbing power as the B.P.C. wool, but is not so white, should be prescribed whenever suitable, as it is less expensive. Unless hospital quality is specifically ordered, however, B.P.C. wool will be supplied. When prescribing elastic hosiery practitioners should specify on Form E.C.10 which of the ten kinds available is required. Prescribers are also reminded that when replacement of a complete colostomy belt or suprapubic belt is needed they should state on Form E.C.10 that a complete outfit is required, otherwise the one part only will be replaced.

# THE ADOLESCENT DELINQUENT BOY

A report on "The Adolescent Delinquent Boy" has been prepared by the Joint Committee on Psychiatry and the Law, appointed by the British Medical Association and the Magistrates Association. It complements the report on "The Unstable Adolescent Girl" published in 1946 (*Journal*, December 14, 1946, p. 909). The report is summarized below.

## More Delinquency Now

The committee found that the problem of adolescent crime was one of great complexity. There has been a steep rise in the incidence of adolescent delinquency in the last 10 years, and the committee thought it probable that there had been a parallel increase in the number of undetected adolescent offenders. The war would appear to have been a major factor, for it led to widespread disruption of family life. An unfavourable feature of the present social situation is the decline in the standards of family life and parental example. There has also been all too often a lowering of the standard of integrity, a lessening of appreciation of moral, social, and spiritual values, and a decrease in the practice of true religion. The war greatly accelerated the development of these changes.

The committee was especially impressed with the need for the guidance of parents and for the prevention, early detection, and correction of disharmonies in the home. The committee felt that ministers of religion can and should play their part in explaining to young engaged couples the meaning of the marriage service and in discussing the responsibilities of marriage. It is also important for the doctor, and especially the family doctor, to play his part in explaining not only the physical side of marriage, but, from his knowledge of the family, to give helpful, friendly, and experienced advice.

It is important that the delinquent who is not likely to respond to any form of treatment should be recognized at an early date after conviction. There is need for thorough research in the problem of the persistent offender, and some new form of treatment or preventive detention may be necessary.

## Bad Homes

Many adolescent delinquents come from homes where conditions are unsatisfactory, and which are overcrowded, inadequately furnished, and neglected. In such a home there is no privacy and no sense of ownership—beds are shared, clothes are shared, the chest of drawers is shared. There is little home life and little opportunity for play. Thus from early childhood the boy is driven into the street, where he is in danger of joining a "tough gang."

There are some particularly bad homes which produce a number of delinquents far in excess of the general relation of delinquents to non-delinquents. Thus a large number of delinquents may come from a small number of "criminal homes," especially in neighbourhoods where moral standards are low. On the other hand some boys from homes of good standard become antisocial because of unfavourable psychological or environmental influences.

The proportion of delinquents who come from broken homes where the parents are divorced, legally separated, or living apart, or where some degree of matrimonial disharmony exists, is high. The boy is often unhappy and insecure. The Legal Aid Act of 1949 enables some of those in matrimonial difficulties to make a free or an assisted application to the High Court for divorce, if it is found that there are sufficient grounds, and there is likely to be a heavy increase in the number of divorce decrees, a fact which will probably have serious consequences to adolescents and children. This state of affairs is all the more serious because, so far as is known, no system has been created whereby those in matrimonial difficulties can receive social help before their cases are examined from the legal point of view. Social help before legal aid is of inestimable value.

In cases of parental disharmony, whether the home is technically "broken" (i.e., where one parent is absent) or

not, one or the other parent may demand too much of the affection or loyalty of the child, constantly trying to impress upon him how much the parent does for him and, therefore, how great is the child's debt. This may lead to rebellion on the part of the child, with consequent delinquency.

### Mothers at Work

The absence from the home of mothers who are working when they are needed by their children has its disadvantages even for the older children. For example, if the mother leaves home for an 8 a.m. shift there is no one to see that the children leave home properly fed, clean and tidy, and up to time. This may be detrimental both to health and to discipline, and may result in bad time-keeping or truancy, or both.

If the mother is not at home when the child returns from school, he often has to stay out in the streets until she returns, and this may lead to undesirable conduct. When the mother does return home, she may be too tired to prepare a proper meal, to give first-aid to tears in clothes and skin, and generally to attend to the welfare of her children. Even more important from the psychological point of view is the fact that she may be unable to listen to the "adventures" of the day and express the sympathy and interest in these which are so important to the child. Therefore he feels unwanted and rejected.

It may well be necessary, in the present economic state of the country, to encourage mothers to return to industry, and many find this necessary on economic grounds. Having worked in factories during the war, some women enjoy the companionship and the relief from the loneliness of being in the house and the monotony of household duties. Furthermore, by becoming wage-earners, wives may be less dependent upon their husbands and on what they may choose to give them from their wages.

A certain number of delinquents are illegitimate, or are born in wedlock where the only reason for the marriage was that the mother was pregnant. In such cases the child may feel, or may be made to feel, that he is unwanted, or even to blame. This feeling may be aggravated where additional children are born in wedlock.

### Adopted Children

Some delinquents are adopted children, and their delinquency may date from the sudden disclosure to them of the fact of their adoption. It is the opinion of many experts dealing with children that, the later the child discovers that he has been adopted, the greater the psychological shock, so that the sooner he learns his true position in the family the better it is for his future security, provided the information is conveyed tactfully. The regulations allowing for shortened birth certificates are of definite benefit and lessen the risk of humiliation. Such certificates can be used as evidence of birth without revealing adoption.

There is a need for the 1949 Rules of the Adoption Act to be amended. Rule 9 (*d*) requires that a notice of application for adoption must be issued to the infant, "unless the Court is of opinion that he is not of an age to understand the effect of an adoption order." Under Rule 32, the notice, which is in a prescribed form, must be served by the guardian *ad litem*. The court has to judge by the age of the infant whether a notice is to be issued to him or not. It is impossible to know from the age as disclosed in the application whether the infant is capable of understanding the effect of an adoption. Thus, there is a very grave danger that the first knowledge that he was not born the son of the adopter might be the receipt of a notice served on a boy by the guardian *ad litem*. The shock might be very great indeed and have a lasting effect on his character.

### Character and Discipline

In many cases the parents of delinquents are of poor intelligence and behave extremely foolishly. Many, through either ignorance or poor mentality, are quite incapable of rearing their children wisely or of good housekeeping. Boys from such homes have "dragged themselves up," their social education has been largely obtained in the streets, and they have had undesirable standards set for them in the home.

It is not, however, the material faults in the environment that primarily, or even mainly, affect the development of character and standards. Personal relationships are more important to the child than material circumstances, and the major environmental factors in the development of standards and character are the degree and type of affection in the family, and the standards of conduct and the example set for the child by his parents. This is proved by the fact that most slum children show no antisocial trends.

Many children have been brought up without any consistent training in self-restraint, and without having acquired the habit of self-control. They grow up with no fixed standard of what is right and what is wrong. The adolescent delinquent has little self-control, so that he takes what he happens to want, without reference to an ethical code of right and wrong, and with little thought for others or for his own future.

Delinquencies may be committed as the result of sudden impulse, or they may be carefully planned. The validity of the plea that a crime was committed as a result of sudden impulse is sometimes called in question, but, nevertheless, it may be perfectly true. Such impulsive actions, however, indicate that the child either has never been taught, or has lacked the ability to learn, to practise any self-control or restraint.

In a few cases of delinquency it is found that the home has a very high standard. Possibly the standards may be too rigid and repressive, so that the boy becomes resentful and rebellious. Some boys elect to lead an antisocial life. The first crimes are often impulsive, but, if the delinquent "gets away with" antisocial behaviour which brings him material profit or emotional satisfaction, he may then plan further delinquencies.

### Intelligence and Education

Many delinquents are below average intelligence. Some adolescent delinquents are to be found in every type of school, although in general they come from secondary modern schools. But the statistical distribution of delinquents between the different kinds of schools is apt to be misleading, since in many of the independent grammar and private schools delinquents are often dealt with by the school authorities, so that they seldom appear in the courts.

Many children and adolescents have suffered from inadequate schooling and were deprived of the stabilizing and socializing influences of school life as a result of wartime conditions. A considerable number are therefore educationally retarded, or even illiterate, because of lack of educational opportunities, although they are of average intelligence.

Truancy from school is often a cause of educational or mental retardation; the converse is also sometimes true. A certain number of boys are deliberately kept away from school by their mothers in order to run errands for them or to look after the younger children. In many cases truancy and delinquency go hand in hand.

The early treatment of truancy is most important. At present, in cases of truancy, the parents are summoned to appear before the magistrates' court, or petty sessional court, and even at those courts where the services of a probation officer are available it is the parent and not the child who can be placed on probation. Usually it is only after the parents have been summoned, perhaps more than once, that the child is referred to a juvenile court, where he may be placed under the supervision of a probation officer. This help and supervision come too late, for by that time he may have become a habitual truant. The boy who gets into the habit of truanting tends to retain the habit when he goes to work.

At present difficulties in the schools are being experienced with a certain number of boys aged between 14 and 15. The group is probably not large, but its members contain some potential or actual delinquents. The boys are usually well- or

over-developed physically. They gain little by the extra year at school, for various reasons, including (i) poor intellectual capacity; (ii) distaste for formal school learning; (iii) overeagerness, characteristic of neurotic boys, for independence and for what seems to them a "grown up" form of life at work; (iv) a genuine precocious maturity coupled with a habit of following their own desires.

The first two factors occurring together are those most commonly found. The boys so constituted naturally become bored with school and are frustrated by the restrictions of school life to a degree that imposes undue strain on their social adaptability, which is often low. Truancy is a frequent outcome and so are such offences as impulsive destruction, impulsive thefts, and mischievous behaviour generally. Moreover, their leisure pursuits are more likely to take a socially undesirable form. When these boys are placed in suitable work this phase usually ends, but if bad habits and companionships have been established, and if the work is unsuitable, they frequently continue.

The fact that the family benefits financially when a child starts working makes some parents aid and abet the older boy in truanting and sympathize with his resentment of school.

It is not suggested that the school-leaving age should be lowered, but it is clearly desirable, especially in rural areas, that the education authorities should endeavour to modify the curriculum so that the interest of these boys may be maintained and so that neither the boy nor his parents should feel that time is being wasted. Such modifications should stress what might be described as "pre-training for work," by providing increasing activities related to these boys' probable working life, in place of scholastic learning, with a deliberate bias towards training in citizenship on a practical basis. Fortunately this has already become a common practice in some areas.

### Work and Play

In general the tendency of the delinquent is to have a craving for immediate high wages. This results in his taking blind-alley jobs. He rarely shows an interest in his work or thought for the future, and, when not dismissed, will change his job frequently without any apparent reason.

The right placing in industry of the below-average boy is most important, and the committee considers that the chances of finding the right type of work for him can be materially increased by full co-operation between the officers of the Youth Employment Service and the headmaster, and especially the form master. In some parts of the country in the past this co-operation has not been adequate and in some cases the boy has been sent to a situation where there happened to be a vacancy rather than to one for which he had some aptitude. When this happens, the boy feels frustrated in this first venture of his life undertaken on his own. It is realized that many of these boys show no special aptitude for anything, and that the Youth Employment Service can act only in an advisory capacity. To most boys the discipline of working conditions comes as a rude awakening.

The policy of the Ministry of Education whereby education authorities, with the co-operation of employers, make arrangements for children to be shown round various local industries in order to broaden their minds, to interest them, and to help them in their choice of career is an excellent one and needs to be encouraged.

The three years between leaving school at 15 and being called up at 18 may be spent most unsatisfactorily unless there is more scientific placing in industry of the type of boy whose instability and lack of concentration are much greater than those of the normal boy.

The normal adolescent usually spends his leisure in a satisfactory way, either as a member of a youth organization, at evening classes, or with his friends at home or elsewhere. As recent surveys have shown, however, even in the case of minor delinquents, the way in which their leisure is spent often leaves much to be desired. It is unusual for a delinquent to be an active member of a youth organization, though he may be loyal to his "gang" to an exasperating degree. Never having got into the habit of doing anything systematically and regularly, except, at most, to attend school by compulsion, he rebels against regular attendance at a voluntary organization.

Gambling plays a large part in the activities of many people to-day. Parents gamble in one way or another and their children naturally imitate them. It may easily lead a boy of weak character to steal and cheat, and is a factor which may produce delinquent behaviour.

Sheer boredom and having nothing better to do may lead many into adventurous exploits which bring them before the courts. The normal boy satisfies his competitive instincts in playing or watching team matches. Others satisfy it by competing against the police and risking detection. Because, after leaving school, so many delinquents take no part in organized games, they rarely shine in any form of sport. But if the delinquent can be persuaded to train seriously for boxing, or athletics, or football, it is not unusual for him to be outstandingly good at it. In addition he learns loyalty to the team and pride in its achievement.

A preliminary report on "leakage" from boys' clubs, in 1947, indicated that, of boys who joined clubs, an average of 39.8% left within six months, and 54% within twelve months. It is not easy to retain as a good member of an organization a boy who first joins when he is leaving or has actually left school. It is therefore desirable that youth organizations should cater specially for boys in the early years of adolescence and while they are still at school. On the other hand boys in the later years of adolescence—between the ages of 15½ or 16 and 18—do not want to spend their leisure with boys who are passing through the crises of the dawn of puberty, so that separate provision should be made for the younger boys. By evoking their loyalty and interest in an organization composed mainly of schoolboys with whom they mix happily while at school, this younger age group will probably transfer without difficulty later on into the organization for older boys which may have attained such a high standard that they would have been afraid to become a member of it when they were younger.

By satisfying the needs of the boys in the early stages of puberty, when they are especially aggressive, destructive, and unstable, youth organizations could do much more than they do at present to prevent delinquency in adolescent boys.

### Solitary Boys

A considerable number of boys refuse to join any organization and may thus get little training in establishing satisfactory human relationships. The solitary boy may be aggressive—the lone wolf type whose aggressiveness has to be expressed somehow or other—and if he cannot find outlet in legitimate ways he is apt to find illegitimate occupation, and appears before the courts as a delinquent. If the parents and probation officers can fully understand the nature and needs of such boys, he may be wisely guided and find salvation, but it will not be by way of youth clubs.

Choice of occupation will be important, and if he has sufficient intelligence and practical aptitude and if some job can be found in which he can do something on his own and express his own individuality, all may be well. If he has committed a serious offence, the difficulty may be great, for such a boy is not likely to be a success in a Home Office school and still less at Borstal, and yet that may be the only available channel of disposal.

The shy solitary child is psychologically even more of a problem than the "lone wolf." He much less frequently comes into the juvenile court, but, if he finds no one to understand him, he may break out into some violent or quite irrational behaviour.

While it is important that attention should primarily be given to the proper treatment of the average boy—and a great deal has already been achieved—the time has come when more serious study of the exceptional should be encouraged.

### Other Failings

The delinquent boy is often generous towards his pals and is generally eager to treat them to cigarettes, to a meal in a café, or to the cinema. A major portion of his money is frequently spent on clothes, usually a suit of the latest pattern and cut, with tie, socks, and shoes to demand attention from the passer-by. A good many offences are committed in order to satisfy his desire to be conspicuous in this way, or to win popularity by bribery, and thereby compensate for his sense of inferiority.

Very few delinquents have a sincere religious background. Such religious training as he may have been given in school has little restraining influence on him, nor is it an inspiration for right doing. It must be admitted, however, that this is frequently also true of the non-delinquent.

Often, because of mismanagement, poverty, and ignorance at home, the health of the adolescent may be inferior. Many neglectful parents fail to have him treated for physical defects discovered at the school medical inspections, and his nutrition often suffers from unwise, inadequate, and irregular meals. In some cases a sense of inferiority arising from a marked physical disability or deformity may be overcompensated by resorting to delinquency.

The cinema is more likely to affect the unhappy boy of poor intelligence. The committee is in general agreement with the Report of the Departmental Committee on Children and the Cinema, which says of the influence of the cinema: "If the values it portrays are wholly worldly and material, the cinema will help to rear a future generation of men and women lacking in ideals of spiritual force and therefore lacking in sound moral standards for normal life."

## RECOMMENDATIONS

### Child Cruelty and Neglect

1. It is essential that there should be early detection in cases where a child is ill-treated or neglected or made unhappy because of unsatisfactory relationships between parents, or between the parents and the child. To assist in this, care committees, as in London, should be established for all schools throughout the country.

2. Where a child's development or happiness is being seriously jeopardized because of physical or mental cruelty in the home, whether direct or indirect, and it is not protected by existing provisions, the children's officer should be notified by either the care committee, the teacher, or the health visitor. The children's officer will frequently need expert medical assistance in dealing with the case, and he is urged to obtain such assistance in all suitable cases. Where the case appears to be hopeless, it should be referred to the police, or local authority, or National Society for the Prevention of Cruelty to Children for inquiry and supervision, and, if necessary, prosecution.

3. Where rehabilitation of the parents is attempted, greater care should be taken to ensure that the child is not subjected to continued neglect or unhappiness while this process of rehabilitation is going on.

4. In cases where children are neglected or made to suffer through their parents' cruelty or lack of capacity to look after them, it is essential that the children should be removed from harm at the earliest possible moment under the provisions of Section 1 of the Children Act, 1948.

### The Adopted Child

5. In cases of adoption, the High Court and County Court judges, and the magistrates in the juvenile courts, should advise the prospective parents to inform the child at the earliest possible moment that he has been adopted.

6. The Adoption Act should be amended so that the age at which an infant is considered old enough to understand the nature of adoption proceedings is determined by the Act, or, preferably, the Act should give to the court a clear discretion as to the service of notice in the case of any infant.

### The Illegitimate Child

7. The mother of a child born out of wedlock should be urged to take care not to ignore or neglect that child after the arrival of a legitimate child.

### Education

8. Under the Education Act, 1944, the special education and care of educable children with low intelligence quotients are fully covered legally. But owing to financial, building, and other current difficulties the necessary and adequate provisions to meet their needs are not yet available. Though a recent increase has been noted, it is urged that an acceleration is imperative if the propensities of this group of children to antisocial behaviour are to be countered.

9. Education authorities should endeavour to modify the school curriculum so that the interest of boys aged between 14 and 15 may be maintained in order that neither they nor the parents should feel that the additional year's schooling is being wasted.

10. Appropriate action should be taken to ensure adequate aftercare of those who leave the special schools for educationally subnormal children.

### Sex Education

11. In addition to giving general instruction in schools in biology (including human reproduction), there is need for instruction in the personal approach in sex relationships.

12. Ideally, instruction in personal sex relationships should be given individually, preferably by the parents. Courses of instruction for parents in the giving of sex education and guidance should be instituted either by local authorities or by voluntary organizations, and efforts should be made to encourage parents to attend.

13. Courses should also be organized for members of school staffs, ministers of religion, and leaders of youth organizations.

14. Advantage should be taken during the period of National Service to encourage young men to adopt the right attitude to the other sex and to impress upon them the sanctity and responsibilities of marriage and parenthood.

### The Adolescent

15. There should be far greater co-operation between the leaders of youth organizations and the parents of the members, and parent-leader associations should be formed for the purpose of discussing the emotional and behaviour problems which arise during adolescence.

16. More home visiting should be undertaken by the leaders of youth organizations.

17. The formation of parent-teacher associations should be encouraged in all schools.

18. It is important that courses in homecraft and mothercraft should be available for girls in evening institutes under the auspices of the local education authorities.

19. In view of the different outlook and characteristics of boys in the various age groups between 13 and 20, the committee feels that clubs should be so organized as to cover the whole range from 13 to 20, but with different sections to cover the different age groups—i.e., 13–15½, 15½–18, and 18–20. These groups should be under the same general leadership and should meet together occasionally.

20. Boys should be encouraged to join a youth organization or club while they are still at school.

21. For boys who are aggressive, and not willing to adapt themselves to ordinary club conditions, experimental clubs might be formed which would cater for spontaneous group formation, with self-government within the group.

### Employment

22. Since a school report on all boys is sent to the Youth Employment Committee, it would be advisable if, in all cases, the committee would consult with parents and school

teachers before the boys leave school and obtain their first situations, and, if possible, keep in touch with the boys afterwards.

23. It is highly desirable that, with the more backward boys, attention should be paid to special placement in industry so that they are not given work which is beyond their capabilities.

24. Aftercare committees should be established in connexion with all secondary modern schools throughout the country.

### Pre-marital Guidance

25. Facilities for obtaining pre-marital advice and guidance should be available to all who desire it. The committee strongly supports the view that education, in the widest sense, before marriage is a vital matter. The family doctor, marriage guidance councils, and the Church are channels through which advice can ordinarily be obtained. The committee feels, however, that with regard to marriage guidance councils, and other lay bodies, there is a real need for a greater measure of selection and training of those giving the advice.

26. There should be a closer follow-up by the Church of those who are married in church, so that the clergy may be on such terms as to be able to advise and help in marital difficulties.

### Married Couples

27. Discord in the home should be dealt with as early as possible, and to this end the committee recommends that those people welcomed in the home, such as the doctor, nurse, health visitor, etc., should be fully cognizant of the help which can be given by psychiatric clinics of the hospitals and child-guidance clinics, by probation officers, or by organizations such as citizens' advice bureaux, the Council of Social Service, marriage guidance councils, family guidance councils, etc. If signs of marital disharmony are apparent, they should encourage individuals to seek the advice of these or similar organizations.

28. The scheme for free or assisted legal aid should be amended so that in some way or other those seeking divorce should be afforded the opportunity of discussion and help from trained social workers.

29. Every effort should be made to help parents to take their pleasures together. To this end, sitter-in services should be established on lines similar to the home-help scheme. The committee realizes that it may be necessary for local authorities to subsidize this service.

30. The home-help scheme should be extended to ensure that no mother resumes her household duties until she has fully recovered from childbirth.

31. Mothers of children of school age should, if possible, be employed only during the hours in which the children are at school.

32. There should be "short stay" crèches, where mothers can leave their children for short periods. This would help to prevent older children being kept away from school to look after the babies.

### General

33. One of the best means of deterring delinquency is the certainty of detection, and this depends on the success of the efforts to increase the strength of the police forces.

34. To enable children who are deprived of a playroom or nursery to have supervised play in surroundings similar to their own homes, and within near reach of their parents, a children's tenement flat should be reserved on the ground floor of new tenement buildings.

35. A distinction must be drawn between the various types of truancy. Where it is due to the child, he should be referred to a juvenile court as soon as possible, and, as in this type of truancy the child is generally maladjusted, there should be further inquiries before a decision on his future is made.

36. The recommendations of the departmental committee on the cinema should be implemented as soon as possible.

### Powers of the Courts

37. Legislation should be introduced to provide for adequate aftercare for those youths who have served a period in a detention centre.

38. Special closed houses, attached to certain approved schools, should be established for persistent absconders. Such houses should be staffed by a team specially selected and trained for the purpose.

39. Special approved schools should be established for the appropriate age groups of severely maladjusted delinquent boys.

40. More hostels should be established for those boys who are found to be maladjusted and are in danger of becoming delinquents.

41. In order to ensure that parents appreciate their responsibilities, a surety should be deposited at the time an order is made under Section 55 of the Children and Young Persons Act, 1933.

NOTE.—Section 55 (2) of the Children and Young Persons Act, 1933, states that "in the case of a child or young person charged with any offence, a court may order his parent or guardian to give security for his good behaviour."

### The Persistent Offender

42. It is important that the delinquent who is not likely to respond to any form of treatment should be recognized at an early stage after conviction. Accurate prediction is essential in these cases, and the committee urges that further research on the problem should be undertaken without delay.

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## THE MENACE OF OVER-POPULATION

### Dr. E. W. BARNES'S CAVENDISH LECTURE

The Cavendish Lecture was delivered before the West London Medico-Chirurgical Society on May 21 by the Bishop of Birmingham, whose subject was "Over-population." Dr. C. E. NEWMAN, president of the Society, was in the chair.

Dr. BARNES, after a reference to Henry Cavendish, eccentric eighteenth-century millionaire and discoverer of hydrogen, in whose honour the lecture had been founded, and to his own friendship with J. J. Thomson and Ernest Rutherford, who were successively directors of the Cavendish Laboratory at Cambridge, spoke of the change of outlook which had taken place in this century concerning the future of mankind. Never had the knowledge of the facts of nature grown so rapidly as during the last 50 years, never had the control over natural processes been so complete, and yet concerning the future of mankind on this earth there was profound pessimism.

In the world at present there were 2,200 million human beings, and the number was increasing steadily and dangerously. In England as late as the time of Queen Anne the struggle between life and death had been severe. Smallpox and other scourges prevailed. When Dean Stanley was at Westminster he opened one of the Stuart tombs and out there tumbled an avalanche of little coffins containing the mortal remains of the 18 children of Queen Anne, only one of whom had lived to be a full-grown child.

The conquest of infant mortality and of disease had been marvellous. Throughout the world populations had expanded. Everywhere communities were becoming disquietingly dense. Pressures arose in many areas from intrusive immigrations, leading to racial enmity. History, as he read it, held little promise for the future of racial groups that were fashioned by overcrowding. Over-population and social progress were not natural allies.

The science of genetics, the Bishop continued, had made great progress during the present century. The nature of Mendelian inheritance had become general knowledge. But what was the effect of the new knowledge? Was it much more than that nature was more powerful than nurture? When an adverse mutation—feeblemindedness was one of the most troublesome—had appeared in a family or group of families it was not removed by transferring those families from a slum into wholesome surroundings. The defect remained, and it was to be eliminated only by eliminating the stock in which it appeared.

### Inferior Stocks

Was such elimination possible without some measure of sterilization or infanticide? What should be the policy of a civilized race anxious to improve the quality of its people? For hundreds of thousands of years the human race had had to struggle to ensure its survival, and thereby it had acquired an outlook which was difficult to set aside, even though religious sanctions were abandoned. The average man—perhaps even more, the average woman—hesitated to admit the legitimacy of any form of euthanasia. Many, perhaps most, would not permit the elimination of defective individuals, even those whose life was a tragic burden to themselves and to the community.

The result of preserving inferior stocks in populations that were becoming excessive was to saddle the community with an increasingly heavy social burden, and probably, as the defective mutations permeated the community, there would be a lowering of the general quality of our people. For ourselves, our food supplies still held out—but was that permanent? Ever larger populations were struggling against one another for food and for space in which to live. Was the process to continue until intolerable conditions made war inevitable? Fifty years ago a few thinkers held that war was a useful blood-letting. We had learned too much of war to tolerate such facile optimism. Atomic weapons were too dangerous to think of their use as a means of eugenic defence. If atomic radiation made for favourable genetic mutations there might be some excuse for such weapons, but, although radiation could produce genetic changes, such changes were almost invariably harmful.

### Birth Control on a National Scale

Until recently it had been held that population increase was necessary for survival in a competitive world. Had not the time come when the wiser leaders of opinion should join in a different policy? There were signs of a change of feeling in France, which continued to be one of the leading intellectual nations of the world, where birth control was a definite element in social policy. In India Mr. Nehru had said recently that the Government was studying the possibilities of birth control. What alternative could there be in a country with a density of 300 to the square mile and where the rate of growth of population in the last 20 years had been three times what it was half a century ago? Japan, realizing that her present food increase was inadequate to her high birth rate, was encouraging contraception and had legalized under certain conditions medically controlled abortion and sterilization. China, on the other hand, was arming her people, but it was difficult to see how, as over-population increased, she could ultimately escape, notwithstanding the very fine qualities of her people, poverty, revolution, and war.

In conclusion the Bishop asked how our so-called Christian country could combine necessary and wise action with what was best in the Christian tradition.

"I do not myself find in that tradition a group of social policies which can be termed final and perfect. How can one expect that in this imperfect world? But I would emphasize that we show loyalty to that tradition when we do our best for those with whom we live, and when we remember the great teaching, 'Thou shalt love thy neighbour as thyself.' Should we not, with the object of increasing the welfare of our neighbours, welcome changes of thought and feeling called for by new world conditions? Should we not join with other peoples in careful thought as to how the moral stature and happiness of mankind can be increased? The ideals we ought to set before ourselves are undoubtedly menaced by over-population. Over-population inevitably leads to the increase of inferior human stocks, which even a few generations ago would not have survived in this country under harsher social conditions.

"What are we to do? Are the great countries of the world to have populations so large that they become an excuse—although a mistaken excuse—for war? Are we to refuse to accept the restraints that limit the increase? Or are we deliberately to seek to foster populations of finer types?"

In moving a vote of thanks to the Bishop of Birmingham, Mr. V. B. GREEN-ARMYTAGE said that so far as he could see it was only the totalitarian State which could deal with this problem, and that meant the destruction of the liberty of man.

## BLINDNESS IN THE COLONIAL EMPIRE

A British Empire Campaign Against Blindness was inaugurated at a luncheon given at the House of Lords on May 23, with the Earl of Halifax presiding and the Prime Minister as chief guest. The purpose of the Campaign is to bring help to people in the Colonies in reducing the heavy incidence of eye disease, which, it is computed, affects between 10 and 15% of the general population. Sir BERNARD PAGET, chairman of the Appeals Council, addressing a conference on the subject before the luncheon, said that in 1945 the Colonial Office and the National Institute for the Blind set up a joint committee to investigate blindness in the Colonial Empire. A delegation made an extensive tour in Africa and the Middle East, travelling 35,000 miles and visiting 12 Colonies. The report they presented revealed a sombre picture, and it was obvious that some action was necessary.

In January, 1950, the British Empire Society for the Blind was incorporated. This body is under the direction of an executive council comprising members appointed by the Secretary of State for the Colonies and the National Institute for the Blind, together with other members having experience in Colonial administration and large-scale voluntary effort. It is empowered to take action in every territory of the Colonial Empire to prevent blindness and to advance the education, employment, and welfare of the blind, and it may extend its working area to the High Commission Territories of South Africa, and any condominium, such as the Sudan, to which the British Government is party. Grants were made to the Society by the National Institute totalling £10,000 for three years, and an even larger sum has been promised by Colonial Governments.

### A Million Blind

Sir Bernard Paget said that it was estimated that a million people in the Colonial Empire are blind, this number being equal to three times the blind population of Great Britain and the United States put together, and that 75% of this blindness and of eye disease in general is preventable. In the four West African Colonies alone the blind population is estimated at 300,000, and East and Central Africa also show very large figures. In Malaya 12,000 blind people have been recorded, and in the West Indian Colonies the incidence again is very high.

The British Empire Campaign Against Blindness (53, Victoria Street, S.W.1), which is being sponsored by the Society, aims at raising this year one million pounds, half of which, it is hoped, will be contributed in the United Kingdom, in certain Dominions, and from selected interests in the United States, and the other half by the Colonies

themselves, each of which has fixed its own target. At present the facilities for educating, training, and employing blind people in the Colonies are woefully inadequate. In all the Colonies there are only 11 schools for the blind, altogether accommodating fewer than 300 children, and with only two small workshops. The work which is to be put into operation as the result of what it is hoped will be a successful appeal will include intensive campaigns in representative regions to demonstrate practical means of preventing eye diseases; continuous publicity to teach people how to preserve their own and their children's sight; grants to voluntary bodies to extend and improve research facilities, eye hospitals and clinics, and to develop existing schools and training centres; the establishment of regional offices, staffed by experts, in each of the principal parts of the Colonial Empire to stimulate and co-ordinate work for the blind by Governments and unofficial agencies; the foundation of at least one school and vocational training centre for the blind in each large Colony, and also centres where local staffs can be trained as school-teachers and craft instructors. Another objective is the establishment of Braille presses to print school textbooks. No Braille books are as yet printed in Colonial languages.

The Society's secretary, Mr. J. F. Wilson, lately visited Nigeria and the Gold Coast to lay the foundations of a West African office and to plan the first ophthalmic survey in the Northern Gold Coast, which includes the "country of the blind," where large numbers of people are afflicted by onchocerciasis.

Lord HALIFAX announced at the luncheon that the blind in Canada, on their own initiative, had launched an appeal throughout the Dominion, sponsored by the Canadian National Institute for the Blind.

## Preparations and Appliances

### PUNCH-HOLDER FOR BLOUNT'S STAPLES

Mr. RANDLE LUNT, M.Ch.Orth., surgeon-superintendent, Bretby Hall Orthopaedic Hospital, writes: The method of obtaining epiphysial arrest by means of the introduction of

stainless-steel staples astride the epiphysial plate described by Blount and Clarke (*J. Bone Jt Surg.*, 1949, **31A**, 464) seems to be gaining favour. The operation is slightly tedious, and accurate introduction of the staples can be difficult. The introduction is facilitated by using the punch-holder illustrated here, which has been made for me by Messrs. Down Bros. With this instrument the staple itself acts as a starter and can often be pushed home to half its length by hand, allowing very accurate positioning. The staple sits in the recess at the end of the holder, and is held firmly in this position by the small spring, permitting withdrawal of the holder when the staple is located in the bone.

An interesting new industrial skin disease is described in the latest issue of the *British Journal of Industrial Medicine* (1951, **8**, 95). It results from continued contact with a vibrating surface—for example, the handling of a lathe standing on a loose floor-board. When the hands have been for some time in contact with the vibrating surface they become red and sweat excessively, and the signs disappear within a week of stopping work. The author suggests the name hyperhidrosis erythematosa traumatica.

## Correspondence

### Hexamethonium and Hemiplegia

SIR,—Recent reports of the occurrence of hemiplegia as a side-effect of therapy with methonium salts prompts me to put on record a further instance of this complication.

A man of 55 years was admitted to Ronkswood Hospital on January 10 with a blood pressure of 270/180 mm. Hg which had been discovered by his family doctor twelve months previously and which had been treated by weight reduction. He was free from headaches but complained of shortness of breath. There were no signs of cardiac failure: the intravenous pyelogram was normal. After five days' bed-rest his blood pressure fell to 236/130. On January 17 the blood pressure had fallen to 200/150 and on that day hexamethonium bromide was started in a dosage of 20 mg. intramuscularly per day. This was gradually increased to 80 mg. per day in one dose, but the blood pressure on January 24 was still as high as 220/150. On that date he suffered from violent vomiting and acute vertigo which did not settle down satisfactorily and the drug was discontinued for two days. On January 27 oral hexamethonium was started (40 mg. four times daily) and continued until February 3, the dosage having been steadily increased to 80 mg. four times a day. The blood pressure was now 230/138—i.e., almost precisely the same as on the first day of administration of this drug. At 4 a.m. on February 4 the patient had a sudden attack of dysarthria with weakness of the right arm and considerable mental impairment. The following day it was clear that he had developed a crossed hemiplegia with a left facial weakness, a much impaired grip of the right hand, and a right extensor plantar reflex. By February 22 gradual improvement had reached the state where movements and power were normal and the extensor plantar reflex had disappeared. The blood pressure remained practically unchanged during this period. By May 16 there were no residual signs of upper motor neurone dysfunction and the patient had been at work for some weeks.—I am, etc.,

Worcester. C. F. J. CROPPER.

### Pentamethonium in Surgical Emergencies

SIR,—Pentamethonium bromide is a new drug and up to the present full use has not been made of its clinical applications. It is known that it will produce, with comparative safety, a bloodless operating field by causing a fall in blood pressure (see R. W. P. Shackleton's paper, May 12, p. 1054). Recently I have been struck by its use in surgical emergencies.

Case 1 was an operation of external ethmoidectomy on a woman in good health. The anaesthetic employed was 0.6 g. thiopentone followed by 60 mg. "flaxedil." An oral cuffed No. 8 Magill tube was passed into the larynx. Maintenance was with gas and oxygen, with further small increments of thiopentone during the operative procedure. As bleeding in this operation is unusually profuse, and we were making a film, 80 mg. pentamethonium bromide was given. This produced a drop in blood pressure from 120/75 mm. Hg to 45/15 mm. Hg *with perfect operating and filming conditions*. The pressure remained at this level throughout the operation, which lasted for 45 minutes. "Methedrine," 10 mg. intravenously and 20 mg. intramuscularly, was given at the end of the operation, with a very speedy recovery of the blood pressure to 100/65. The patient was returned to the ward in good condition and semi-conscious. During the night severe haemorrhage occurred and a new resident dealt with the condition very effectively but in quite an unorthodox manner: to wit, by administering 50 mg. pentamethonium bromide intravenously. This controlled the bleeding, but unfortunately no record of the blood pressure was taken. When seen by myself the following day the patient was very well, there was no recurrence of the haemorrhage, no ill effects were obvious, and her complete recovery was uneventful.

Case 2 was a high and difficult gastrectomy done on a fit young man. The anaesthetic consisted of thiopentone, gas–oxygen–cyclopropane, with tubocurarine as a relaxant. Towards the end of

the operation the ligature on the left gastric artery slipped and profuse haemorrhage occurred: this was controlled by packs. It was felt, however, that it would be extremely difficult to catch and tie the bleeding point owing to its inaccessibility. After consultation it was decided to give pentamethonium bromide; 90 mg. in all was given intravenously in split doses over a period of 8–10 minutes, bringing down the blood pressure from 100/75 mm. Hg to 50/30 mm. Hg. The packs were then removed and the bleeding was found to have stopped: in fact the bleeding point could not be found. The problem then arose whether to close the abdomen with or without a pack, or to bring the blood pressure up before closing. The latter was adopted, 30 mg. "methedrine" being given intravenously with a recovery of the blood pressure to 100/75 within a few minutes. There was no further onset of haemorrhage, and the abdomen was closed. The patient made an uneventful recovery.

Judging from these two cases it seems to me that the use of this drug in the control of haemorrhages offers possibilities which would bear investigation. I have in mind (1) ligature or forceps slipping on a renal pedicle, (2) arterial anastomosis, (3) post-operative haemorrhage, (4) ordinary emergencies like haemoptysis or haematemesis. I must stress, however, the importance of the fact that none of these trials be made by anyone other than a skilled anaesthetist, fully conversant with modern measures of resuscitation, and only in selected cases.—I am, etc.,

London, W.1. J. KENNEDY HARPER.

### Is Superinfection Important in Tuberculosis?

SIR,—In your answer to a correspondent ("Any Questions?" May 19, p. 1153) you write that the main body of tuberculosis mortality in Great Britain "results not from primary infection but from superinfection occurring at some later date." You may be right, but I think your correspondent should know that there is a substantial and I believe growing number of phthisiologists to whom superinfection appears of little importance. To them phthisis develops from the primary lesion, or from the seedings of the haematogenous dissemination which usually occurs shortly after primary infection.—I am, etc.,

Aylesbury. STEPHEN HALL.

### Pethidine Sensitivity?

SIR,—As a frequent employer of pethidine in conjunction with nitrous oxide–oxygen anaesthesia, I was interested to read the description of Dr. A. L. Reynard's case (May 12, p. 1081). I feel, however, that in his interpretation of the events described I can agreed with him only as far as the termination of the operation, which he states was approximately 45 minutes after the second intravenous dose of pethidine.

That pethidine depresses respiration is generally agreed, but before holding it responsible for the severe collapse described, and so long after injection given intravenously, I feel that one must consider the possibility of other contributing factors. I cannot help wondering whether there was not some degree of respiratory obstruction present after the patient's return to bed, for in the presence of a slightly depressed centre this could itself give rise to just such a train of events as described, and the resultant damage to the medullary centres from prolonged hypoxia would account for the delayed response to resuscitation.—I am, etc.,

Hitchin. O. H. E. BAYLES.

### Intravenous Pethidine

SIR,—Following the introduction of intravenous pethidine as an adjuvant to general anaesthesia by Mushin and Rendell-Baker (*British Medical Journal*, 1949, **2**, 472) there have appeared in your columns two case reports of so-called "pethidine sensitivity" (Zuck, January 20, p. 125, and Reynard, May 12, p. 1081). Both cases were characterized by acute generalized shock, the first exhibiting tachycardia and the second a marked bradycardia. While in the first case the rapid onset of symptoms may have indicated a condition of true generalized pethidine sensitivity, Dr. Reynard's case is strongly suggestive of a direct cardiac effect of the drug. Dawes (*Brit. J. Pharmacol.*, 1946, **1**, 90) has demonstrated the quinidine-like action of pethidine on the isolated rabbit auricle, which is exerted in a potency of 0.83 times that of quinidine itself, weight for weight. That intravenous pethidine can induce heart block in the artificially respiring cat has been demonstrated in the Department of Pharmacology, University of Leeds.

In view of the accompanying bradycardia, it is thus possible that Dr. Reynard's case may have been, in fact, one of hypersensitivity to the quinidine-like action of pethidine. I feel that his suggestion that intravenous pethidine has little place as a routine anaesthetic agent might profitably be extended to include the intravenous use of the drug in general.—I am, etc.,

Leeds. K. A. EXLEY.

### Obstinate Tapeworm

SIR,—In his reply to the questioner who had failed four times to dislodge a tapeworm with filix mas, your correspondent ("Any Questions?" May 19, p. 1154) did not mention a useful and not unpleasant treatment—namely, mepacrine. I have found it expel the head in a dosage of 1 g. given in two cachets after the usual preparation. The worm is stained bright yellow and so recognition of the head is easier.—I am, etc.,

Enfield, Middlesex. C. ALLAN BIRCH.

SIR,—I should suggest giving the filix mas through a Ryle's tube. Use the ordinary preparation, and on the second day pass a Ryle's tube. Wait till the end is in the duodenum (turning the patient on his right side helps). Then, when *x*-ray screening shows the end in place, give through the tube a drachm of liquid extract of filix mas made up to about 10 ml., followed by about 5 ml. water.

This gets a concentrated dose of filix mas well on to the head of the worm. I have found this method succeed several times after other ways had failed.—I am, etc.,

King's Langley, Herts. REGINALD FISHER.

### London School of Hygiene Association

SIR,—A school association has been formed, membership of which is open to all students who have followed a complete recognized course of instruction in the London School of Hygiene and Tropical Medicine. There is a nominal entrance fee of 2s. 6d. but no annual subscription. Members are entitled to receive every year a copy of the annual report and any notices connected with the association. It is hoped to arrange an annual open day and possibly an annual dinner. A special association tie has been designed, and is obtainable at a cost of 17s. 6d.

I hope that all past students will join the association and maintain as close contact as they can with the school and staff. Applications, together with the entrance fee of 2s. 6d., should be sent to Miss K. M. Shaw, Personal Assistant to the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1.—I am, etc.,

London, W.C.1. ANDREW TOPPING, Dean.

### Gallamine Triethiodide and Electro-convulsive Therapy

SIR,—The papers by Drs. O. S. Thompson and A. Norton (April 21, p. 857) and by Drs. R. H. F. Smith and D. L. C. Thomas (p. 860) on this subject were of great interest. We should like to confirm and comment on their findings from our experience of 110 treatments on 16 patients aged from 23 to 73.

We first used a method very similar to that of Drs. Thompson and Norton in March, 1950, for a young man, a schizophrenic, who had shortly before suffered a crushed dorsal vertebra in an unmodified induced fit. So pleased were we with the result that we have modified all E.C.T. since with "flaxedil."

For the first treatment the dosage is judged on the experience of one of us as an anaesthetist and is suitably modified for the later fits. The range has been 60–80 mg. flaxedil mixed in a syringe with 250–500 mg. thiopentone and 1/100 gr. (0.65 mg.) atropine sulphate. The patient lies in bed with his head on one pillow. One nurse gives all the assistance needed and remains with the patient until he recovers. No restraint or special padding is needed. The injection is given and as consciousness is lost the apparatus is carried into the room. The lungs are gently inflated once or twice with oxygen from a face-mask and bag, and after about two minutes the shock is given. The stages of the convulsion are recognizable, the clonic stage varying from a slight twitching to a definite convulsion in which, however, the muscles offer no resistance to passive movement. The chin is supported throughout, and on the slightest sign of cyanosis the lungs are, even during the fit, again inflated. Cyanosis is rare, owing to the initially high alveolar oxygen. On cessation of movement the lungs are again inflated and the patient turned on his side. This obviates any need of an artificial airway and prevents inhalation of the saliva that is often produced. The duration of apnoea after the fit is oddly constant for each individual in all his treatments and occurs even if the shock is delayed until reasonable respiration has returned after the injection. If there appears to be any risk of the patient waking when partially paralysed we give 1.25 mg. neostigmine intravenously. All our patients have woken quietly, as if from a natural sleep, within twenty minutes. One elderly woman failed to convulse after either modified or unmodified shock.

After this admittedly short series we feel that it is becoming clear that the method has the following advantages: (1) Feeble muscular action, causing neither local damage nor systemic strain. (2) Absence of glottic spasm and prolonged respiratory depression, making the avoidance of anoxia simple. (3) Full psychiatric effect of the treatment enhanced by the fact that the patient, often anxious and depressed, sees no apparatus but a syringe, feels nothing worse than a thiopentone induction, and awakes quietly and orientated. The increasing confidence of most patients contrasts markedly with the sometimes increasing fear of unmodified electroplexy as the course proceeds.

We believe the method to be effective, safe, and speedy. It should not be undertaken without apparatus for pulmonary inflation nor without the immediate availability of instruments for intubation and resuscitation and the presence of someone skilled in their use. Whenever a patient is rendered unconscious and apnoeic, accidents can happen. The contraindications are those of barbiturate anaesthesia and the curarizing drugs.

The observations of Drs. Smith and Thomas on the effects of flaxedil on conscious patients are of importance as an investigation, but we feel most strongly that no patient should ever be subjected to curarization when conscious. We have recently heard from a reliable source of patients fearing surgical operation because of true stories of the awful feeling of "waking death" following the anaesthetist's injection. To subject psychiatric patients to such an ordeal cannot be helpful. The raised blood pressure and respiratory rate found by these investigators might surely be due to anoxia as well as to fear. Thiopentone would be expected to lower the blood pressure and slow respiration without, however, relieving the anoxia.

Some queries may be added on the psychology of E.C.T. If, in contrast to insulin, cardiazol, or unmodified E.C.T., patients can be made unaware of the whole procedure (one of our patients thought that there was nothing happening but the injection), how does this affect the psychological interpretation of the convulsive reaction as the experience of, and unconscious need for, punishment against guilt-feeling? If, as seems agreed, results of modified E.C.T. are at least as good as unmodified treatment, are we still right in interpreting after-shock aggressiveness in unmodified treatments as abreactive? Or can the absence of post-convulsive excitement, even after the effect of thiopentone and relaxant has worn off, be co-ordinated with the quicker return to normal of the electroencephalogram after shock under an anaesthetic?—We are, etc.,

W. M. JONES.
H. B. ROSENBUSCH.

Harrogate.

## Diet in Diabetes

SIR,—The paper of Drs. C. C. Forsyth, T. W. G. Kinnear, and Professor D. M. Dunlop (May 19, p. 1095) is of great importance in drawing attention to the necessity to provide the diabetic, and particularly the diabetic child and the pregnant woman, with a diet adequate to maintain proper nutrition. That this can be effected by "free" diet is not, however, by any means established. Such a diet had to be abandoned in 11 of their 50 cases, and "the fact that failures are still appearing after five years' treatment is disquieting." On the other hand the condition of patients on their controlled diet was generally less satisfactory as judged by body weight. But surely the controlled diet contained far too little carbohydrate. Presumably their cases were of similar type to those studied on a "free" diet, who were non-obese diabetics, males preponderating in the ratio of 2 to 1, and whose occupation ranged "from sedentary work to heavy labouring." Yet 30 of their 39 patients received only 150–200 g. carbohydrate, and seven even less.

One would agree with their conclusion that diabetics who have never been overweight may be given a full diet without much danger of becoming obese, but in some cases a tendency to exceed the desirable weight must be checked by dietary restriction. For several years it has been my practice to commence treatment of the non-obese patient with a measured intake of carbohydrate, 200–250 g. for a woman, 250–300 g. for a man, allowing free choice of protein and fat. Glycosuria is controlled with insulin, and the adequacy of the diet judged by the patient's appetite and the weight. The dietary carbohydrate is adjusted so that the patient is satisfied and the diet approximates closely to that of other members of his household, but few desire more than 300 g. Insulin dosage is altered as found necessary. Thus the patient is very soon taking a diet virtually of his own choice, glycosuria being generally controlled with one injection, usually a mixture of soluble and P.Z. insulin. With this regime he is less liable to insulin reactions, and is also able to make adjustments in the amount of insulin when upset by intercurrent illness. He is told what is his "ideal" weight, and instructed that this must never be exceeded. This method is simple and generally ensures the full co-operation of the patient, and appears to me preferable to the "free" diet. It is of interest to note that the great majority of the patients of Drs. Forsyth, Kinnear, and Professor Dunlop on "free" diet were found to consume between 200 and 350 g. carbohydrate, just the amount in the controlled diets of my patients.

In conclusion I would like to refer to the term "correct" weight. Published tables of average weights are satisfactory for men and the younger female age groups, but the "average" weights given for women of middle age or more are undoubtedly above the "desirable," probably by about 10%. It is noted that two women in the authors' series had formerly been overweight, and that "free" diet had to be abandoned as they again became obese. This is surely what might have been anticipated. With a history of obesity, dietary restriction is probably always necessary, and generally this is effective without resort to insulin.—I am, etc.,

Glasgow. IAN MURRAY.

## Polymastia and Breast-feeding

SIR,—I have read with interest the case of "Polymastia Observed in Pregnancy," reported by Dr. F. Hamilton Leckie (May 12, p. 1060). Dr. Leckie remarks that in a case of this nature breast-feeding is probably contraindicated, since he argues that the flow of milk from the supernumerary breasts would probably continue even though the extramammary glands were not suckled. This may be a fallacious conclusion, as in the case reported the supernumerary nipples were suckled. One other case which I have seen lends support to this view.

A primigravida was observed to have islands of additional breast tissue, with a rudimentary nipple in the region of the right

axilla. She was delivered normally at term, following which lactation became established, and milk was seen to drip freely from the additional nipple during breast-feeding. No attempt was made, however, to put the child to this nipple, and after the first five or six days of the puerperium the flow of milk from it became markedly decreased, and disappeared entirely by the twelfth day, when the patient was discharged from hospital. The supply of milk from the normal breasts continued unchanged.

It is possible, therefore, that the attempt to feed from the additional nipples in the case reported by Dr. Leckie was responsible for continuation of the milk supply, which might have dried up had suckling from them not been attempted.—I am, etc.,

Manchester. C. J. DEWHURST.

### Insomnia after Tuberculous Meningitis and Streptomycin

SIR,—In answer to Dr. Charles Weston's letter (May 12, p. 1081), we have not in our series of cases noted insomnia as an after-effect of tuberculous meningitis treated with streptomycin. During the course of treatment sleep abnormalities have been noted, including complete reversal of sleep rhythm, but these have, in our experience, all resolved with recovery. We have noted as an after-effect in treated cases disturbances which are presumably due to lesions of the hypothalamus or its neighbourhood, such as obesity and glycosuria, and there seems to be no reason why insomnia should not also occur, as in Dr. Weston's case. It is a recognized sequel of other neurological disorders involving this region. One would have thought that there was no objection to barbital therapy, but some of these cases learn to lead lives consistent with their new sleep pattern.—We are, etc.,

W. L. CALNAN.
J. RUBIE.
A. F. MOHUN.

London, S.W.3.

### Oral Streptomycin for Dysentery

SIR,—For some months now, with the co-operation of the physicians, at the Peace Memorial Hospital we have been using streptomycin orally for the treatment of Sonne dysentery, in which in quite a large percentage of cases courses of sulphonamide drugs have proved ineffective. The dosage usually employed is 0.5 g. twice daily for four days. Stools are tested 48 hours after cessation of treatment, and again at periods up to one month, and have remained negative for *Shigella sonnei*. Clinical response was equally rapid, with no subsequent remission, in the 20 cases tested so far. There have been no toxic manifestations, as would be expected, since the drug is not absorbed from the gut. All strains were tested for sensitivity prior to treatment, and to date we have not isolated a resistant strain.

An argument has been put to us that, should a patient have a quiescent or undiagnosed tuberculous lesion, streptomycin-resistant strains of tubercle bacilli might develop from this treatment. As the drug is not absorbed in the gut we think this criticism is without foundation.

We have not found any record in the literature of oral streptomycin trials in this country, but Ross *et al.* (*J. Amer. med. Ass.*, 1949, **141**, 183) report satisfactory results in the treatment of Shigella enteritis with oral streptomycin.—I am, etc.,

Watford. B. A. THOMPSON.

### Chloramphenicol in Persistent Dysentery

SIR,—The recent memorandum by Drs. D. A. Sime and D. Cameron (May 5, p. 997) confirms the experience gained in a children's hospital and a children's ward of a general hospital during an outbreak of Sonne dysentery. Forty-six out of 48 cases were treated first with one of the generally used sulphonamides. Those patients who became clinically symptomless, but whose stools remained positive, were sent home or transferred to an isolation hospital. This, however, was impracticable in seven cases, all of which were subsequently treated with chloramphenicol. Three of them died of the illness for which they were admitted originally. The remaining four became negative, three after one course of 100 mg./kg. body weight daily in divided doses for four days, and one after two courses. All of them showed three or four consecutive negative specimens taken at intervals from five to seven days. The two cases not treated with sulphonamides became and remained negative after one course of chloramphenicol.—I am, etc.,

Brighton. W. MESTITZ.

### Treatment of Orf

SIR,—Dr. G. M. Lloyd (May 19, p. 1144) writes, "The condition resolves itself in five to eight weeks, as reported. Treatment with the earlier antibiotics has been unsatisfactory." Perhaps it may be of some help in other cases to report that during the last few months I have treated three cases of orf with ung. hydrarg. ammon. dil. In each case after three days of this treatment there were no further signs of activity and the exhibition of a bland ointment resulted in a healed lesion at the end of another seven to ten days.—I am, etc.,

Cheriton Bishop, near Exeter. F. E. GRAHAM-BONNALIE.

### Atropine and Whooping-cough

SIR,—I was very interested to read Dr. E. M. Singer's letter (May 19, p. 1145), in which she mentions a case of atropine poisoning following 10 ml. of atropine methonitrate and recommends that for home use an aqueous solution be prescribed. Apart from an unsuccessful attempt at suicide, by an adult, this seems to be the first recorded case of poisoning, and, as Dr. Singer says, atropine methonitrate has become increasingly popular of recent months as symptomatic treatment for whooping-cough. The use of an aqueous solution presents some difficulties, because a 0.6% solution (or a 1:10,000 solution, commonly employed in treating infantile pyloric stenosis) will not keep satisfactorily for more than a few days, and repeat prescriptions would place an added burden on the pharmacist. Moreover, accurate dosage with the last-mentioned dilution, in terms of portions of a teaspoonful, is not possible. It seems far more likely, too, that a good portion of an alcoholic solution would be spat out by a child because of its very unpleasant taste, whereas an aqueous one is practically tasteless. The answer seems to be, as always, that drugs in any form should be kept out of the child's reach.—I am, etc.,

London, W.C.2. J. R. COX.

### Child Health Visiting

SIR,—Professor A. G. Watkins's report (May 12, p. 1075) on the work of health visiting in a children's department is of great interest, as I have had what I think is probably the unique experience of having worked for two years in a university neonatal department to which a health visitor was attached, and then became responsible for similar cases in a general practice to which again a health visitor was attached.

This idea of elaborating and perfecting home visiting from a hospital in the case of children passes by the very foundadation of any principle of paediatric treatment—namely, that, ideally, children should never reach hospital but be treated in the home and nursed, if humanly possible, by the mother. When I first qualified and became a house-physician in a university children's department this was one of the lessons continually instilled into me by a chief whose teaching has been my inspiration ever since. During my succeeding six years in paediatrics it has become more and more obvious that children recover more quickly and are far happier at home. The more enthusiasm and conviction about this, the easier it is to find ways and means to avoid admission to hospital. It is now perfectly obvious to me that less than a quarter of present admissions to children's wards are really necessary. Thus the whole idea of home care by health visitors from a hospital following hospital

treatment is putting the cart before the horse. Far better would it be to extend the scope of the domiciliary consultant service in paediatrics so that, when the general practitioner found that he required expert help, the specialist could not only visit once and give his opinion and advice but if necessary follow up in the home, working with the general practitioner. He then could, if he wished, either use a health visitor attached to the general practitioner or, if the treatment required was of a highly specialized kind, provide his own personal health visitor.

All health visitors with whom I have had any dealing are unanimous in saying that they would far rather work in conjunction with one individual doctor than be given a list of people who must all have routine visits whether they require it or not (as they are required to do by local health authorities). Then all their visits would be to those who are in need of help. So it seems to me that it would be very much closer to the ideal so far as paediatrics is concerned if health visitors worked primarily as part of one particular general practice, or in partnership with a consultant working in domiciliary paediatrics but with a scope far greater than is possible to-day. Thus, if he so wished it, any individual general practitioner could enlist far greater help with treatment in the home and so avoid parting the child from his parents. This makes allowance for the general practitioner who is himself vitally interested in the care of the children in his practice and also for those who feel that they cannot cope with children efficiently.—I am, etc.,

York. SHEILA F. SCHOFIELD.

### Frequency of Mosquito Bites

SIR,—Dr. R. C. Muirhead-Thomson in his paper (May 19, p. 1114) on "The Distribution of Anopheline Mosquito Bites Among Different Age Groups" does not indicate whether he considers that the surface area presented by the mosquito's victim has any influence on the number of times that he or she is bitten. While the question of surface area is probably unimportant for a comparison of bite frequencies between adult male and female subjects it should surely be involved for any adult/child comparison. In this connexion a more direct comparison for all figures could be made if the weights of the subjects were given. This would allow for evaluation of relative surface-area figures and the "bites per unit area."—I am, etc.,

London, N.14. EDWIN R. NYE.

### Medical Work in New Guinea

SIR,—This letter is an appeal to young graduates to consider doing medical work in New Guinea. It is difficult to explain how great the need is to people who have not seen the condition of the natives in New Guinea.

The work is demanding, because the jungle people will not go to the doctor readily: they are too afraid of the witch-doctor on the one hand and of the unknown white man on the other (until they gain confidence). When they do appear their condition generally requires immediate attention, and the result can easily mean the difference between life and death. But the chronic diseases, also, are rife: hookworm, yaws, malaria, tuberculosis, dysentery, skin diseases, tropical ulcer, undermine the health of the whole people, as do their lack of understanding of an intelligent diet, and the absence of any glimmer of an idea about hygiene. The villages are generally filthy, where a crowd of half-wild pigs and starved, diseased dogs wander about.

In a country of low moral and physical standards the women are the most miserable. They eat what is left when the men have finished; they do the heavy work; they are bought, sold, or exchanged at the whim of the men, by whom they are ill-treated with impunity. It is not surprising that newly born children have often little chance of survival, even if they are wanted. If they are not, they are knocked on the head and thrown out.

A few days ago I was in a district in this delta of Papua where there are 1,500 people who must travel for a day to get medical help. After paddling for a whole day they reach a "medical assistant" (six months' training) and a native orderly. There is no doctor. This district is not unique nor even unusual.

I believe that there are over 50,000 medical men and women in Great Britain. If only a dozen of them would leave their congested areas to work in New Guinea the amount of good they could do is incalculable.

Life here has its compensations. After a few years the medical man has the satisfaction of seeing the villages cleaned up, the hordes of miserable dogs eliminated, the population increasing and their physique improved, and the confidence of the local people in the white doctor gained by modern methods of treatment and cleanliness. Perhaps, too, a growth of some idea of compassion both for each other and for the rest of the animal creation may result.

And the country is beautiful. The mountains, the trees, the flowers, the birds, the fireflies and butterflies, the sunny climate, must be a source of happiness to most educated people living in this country. Also many pests that civilized people have organized for themselves—shortages of everything (except regimentation and frustration), strikes, black-outs, and the income tax—are missing here.

A letter to the Director of Public Health, P.H. Dept., Port Moresby, Papua, New Guinea, will bring particulars of conditions of service, salary, etc. Several missionary societies have centres here. The Rev. N. F. Cocks, Australasian Secretary of the London Missionary Society, is at present in England, and application can be made to him at Livingstone House, Broadway, London, S.W.1, for any information required about work in Papua.—I am, etc.,

Aird Hill, Delta, Papua, New Guinea. E. K. MACKAY.

### R.M.B.F. Appeal for Clothes

SIR,—We would like to remind your readers of the work we do, in the Clothes Room, for the widows and children and dependants of the less fortunate members of the profession. In these times, when prices are steadily rising, the lot of those who have met with misfortune through no fault of their own is critical, and the number of applications for help with clothing has risen sharply. Particularly mothers with growing children, though often in sore need themselves, are happy and content if we can help with their family.

We are in constant need of clothing of all sizes, winter and summer, for men and women and children of all ages. We have special facilities for cleaning when necessary, and we should be very grateful for any gifts, which should be sent direct to: The Clothes Room, The Ladies' Guild of the Royal Medical Benevolent Fund, Tavistock House North, Tavistock Square, London, W.C.1.—We are, etc.,

DOROTHY MORAN,
President.
J. M. BANISTER,
Chairman, Clothes Committee.

London, W.C.1.

## POINTS FROM LETTERS

### Vitamin C and Allergic Rhinitis

Dr. F. CORT (Whitburn) writes: With reference to this subject ("Any Questions?" May 19, p. 1154), vitamin C is only associated with the prophylactic treatment of allergies and allied conditions such as the common cold. Ascorbic acid will not abort either an allergic rhinitis or a common cold once histamine activity has occurred, and its entire role is in the prevention of such histamine activity. In my view it achieves this in probably two ways: (1) It assists the liver to store additional glycogen reserves, thereby preventing excessive protein breakdown and subsequent excessive amounts of intracellular histamine; (2) it tends to reduce the sensitivity of the mucous membranes, thereby reducing the degree of vasomotor reaction to irritants. I have seen several cases of allergic rhinitis, where attempts at desensitization to a specific allergen have failed, kept free from further attacks by the use of massive doses of ascorbic acid, together with regular daily doses of glucose. It is also wiser to reduce the protein intake in the diet and provide for the abortion of the attack by the use of an antihistamine and vasoconstrictor intranasally.

# Obituary

## R. St. A. HEATHCOTE, D.M., F.R.C.P.

Dr. R. St. A. Heathcote, professor of pharmacology in the Welsh National School of Medicine, died in University College Hospital, London, on May 19, in his 63rd year.

Reginald Saint Alban Heathcote was born in 1888, youngest son of the Rev. G. Vyvyan Heathcote, of West Deeping, Lincolnshire. A scholar of Winchester and New College, Oxford, he went on to University College Hospital as the first holder of the Theodore Williams Scholarship. Graduating just before the first world war, he saw service in the field as a captain in the R.A.M.C. until 1917, and then until the end of hostilities as a surgeon-lieutenant, R.N.V.R. Returning to Oxford, he joined the staff of Professor J. A. Gunn in the department of pharmacology, and proceeded D.M. in 1920. Two years later he took the degree of B.Sc. It was at this time that he began to publish the first of a continuing series of papers which were to become known for clarity and thoroughness.

In 1922 Heathcote went to Egypt as first occupant of the chair of pharmacology in the University of Cairo, at the age of 34. His broad academic training, great mental powers, and enthusiasm for teaching and research work fitted him well for this responsible post. There, besides occupying a prominent position in the life of his countrymen in Egypt, he bore the main burden of organizing a modern department of pharmacology, training and encouraging assistants who have since played a major part in local developments in this subject in their country. He took an important place in the Congrès International de Médecine Tropicale et d'Hygiène in 1928. Travelling widely, he developed an enviable ease in expounding the fascinations of the antiquities of Egypt, and he possessed a superb collection of photographs which he built up over the years. For the work he did for the University of Cairo he was appointed to the Order of the Nile. In 1932 he became a Member of the Royal College of Physicians, and a Fellow five years later.

Returning to this country in 1933, Heathcote was appointed independent lecturer in, and subsequently professor of, pharmacology in the Welsh National School of Medicine at Cardiff. There he remained until his death, building up his department, writing a series of excellent articles in the *Medical Annual* from 1937 to 1946, pursuing important researches in pharmacology in relation to invertebrate animals, playing a vigorous part in the Home Guard during the last war, and endearing himself to a generation of Welsh students of medicine and pharmacy by his amiability and profundity. A man of great personal charm, witty, amiable, with an astonishing memory, wide knowledge of academic affairs, of his special science, of art and history, he had many sides to his character. He was a gourmet with an admiring appreciation of much that is best in France, and a skilled worker in metal and wood. He was gentle and encouraging with beginners, penetrating in his analysis of the work of those more experienced, sane and cautious in his opinion of research matters, loyal to his friends, and discreet in committee. His wife, who was the youngest daughter of Osbert Salvin, F.R.S., died in 1947. They had one son, who survives them.—J. D. P. G.

## JAMES BATTERSBY, F.R.C.S., F.R.F.P.S.

Dr. James Battersby died at his home in Helensburgh on May 20 at the age of 80. The announcement of his death will bring back many memories to Glasgow graduates all over the world, and especially to those who received their medical education at St. Mungo's College or who were in any way associated with the Glasgow Royal Infirmary.

Battersby qualified in Glasgow, taking the triple qualification in 1896. After holding the posts of senior house-surgeon and house-physician at the Royal Infirmary he obtained in 1899 the F.R.C.S. (England), being one of the first men north of the border to hold this distinction. He became a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow in 1907. For many years he held the position of professor of anatomy at St. Mungo's College and combined with this an appointment on the surgical staff of the Glasgow Royal Infirmary, where he was an assistant surgeon. He ran a general practice in the east end of Glasgow in addition to his specialist appointments, and retired from this in 1934. An excellent teacher of anatomy, he was renowned for his blackboard drawings. Despite his many and varied medical interests, he managed to find time to take part in civic activities, having been collector and deacon of the Incorporation of Barbers of the Trades House of Glasgow—a body with which doctors have been associated for generations. He was also a keen Mason and a member of the Society of Antiquaries of Scotland. His work for the B.M.A. extended over many years. He was honorary secretary of the Section of Anatomy at the annual meeting in 1922, a representative of his Division for several years before the last war, and president of the Glasgow and West of Scotland branch from 1945–9.

Battersby was a remarkable man in many ways, but principally, perhaps, in his ability to overcome the disadvantages of a frail physique which would have handicapped many men of lesser courage. He was adored and admired by many generations of patients and students, to whom he was known affectionately as "Wee Jimmie." A "character" in the true Scottish sense of the word, his kindliness and pawky sense of humour will never be forgotten by those who knew him. By his passing a link has been severed with an older and entirely different generation of practitioners. We extend our sincere sympathy to his wife and three sons.—G. H. S.

## Sir WILLIAM GOODENOUGH

Sir William Goodenough, who died on May 23, was one of those men of whom there are so many examples in the British tradition who crown an eminent career in business with another career, as arduous and calling for similar qualities, in social service and public life. Oxford was his university and also the place where he entered upon his career as a banker, and there he soon made his mark. In him Lord Nuffield found the ideal pursebearer in those benefactions which startled the country in the years before the last war. Sir William Goodenough became chairman of the managing trustees of the Nuffield Foundation, of the Nuffield Trust for the University Medical School, of the Nuffield College, and the Nuffield Dominions Trust. He had more to do than most with the shaping of the Nuffield Provincial Hospitals Trust—a body which carried on in the provinces the kind of work which the King Edward's Hospital Fund was doing in London. For nearly

twenty years also he was curator of the University Chest, and for an even longer time treasurer of Radcliffe Infirmary. In his work for hospitals he inherited the zeal of his father, the late F. C. Goodenough, whom he succeeded as joint honorary treasurer of the new Westminster Hospital. He was also treasurer of the British Postgraduate Medical School and of the Medical Research Council. In all these positions he brought to bear his conspicuous ability in financial administration and a far-sightedness which was of the greatest value in a time of hospital transition. Like Lord Beveridge and others, he achieved immortality by the attachment of his name to a famous report. In 1942 he was appointed chairman of an interdepartmental committee set up to inquire into the organization of medical schools. The committee took important evidence and produced a report which was hailed in many quarters as presaging a new era in medical education, though its recommendations did not escape criticism. One of the proposals which it elaborated was that a period of clinical experience under supervision in hospital should be an integral part of the training of doctors after qualification; effect has been given to this in the Medical Act, 1950, and on the very day of Sir William Goodenough's death the General Medical Council was framing regulations to meet this requirement. A man of high ideals and strong convictions, and of fearlessness in the expression of them, his death at the early age of 52 is a great loss not only to the banking community but to the world of philanthropy and education.

## J. R. C. GREENLEES, D.S.O., M.B.

R. W. C. writes: As a family doctor Greenlees was trusted and beloved in a very exceptional degree. He took a great interest in children and in the welfare of youth. For seventeen years he was assistant physician to the Royal Hospital for Sick Children, Glasgow, and held a similar post at the Western Infirmary. In 1926 there came a major change in his life's work. The governors of his old school of Loretto, having to appoint a new headmaster, and being impressed by his strength of character, his personality, and his understanding of boys, took the unusual step of appointing him as headmaster. If there was some surprise in educational circles at the appointment of a medical man to this important scholastic post, it was quickly dispelled. His appointment was an outstanding success. His fine presence and impressive personality made a great impression on the boys, who were devoted to him. He made it a point to know each pupil intimately. He was kind and understanding, but was also a strict disciplinarian. Slackness was a thing he could never tolerate. A man of strong religious beliefs, his main object as headmaster was the building of character. He retired from the post in 1945.

Greenlees, however, always retained his interest in medical affairs. He served for some years as a member, and later as chairman, of the board of management of the Royal Hospital for Sick Children, Edinburgh. His tireless energy and drive were of great benefit to this institution. When the National Health Service Act came into operation the Secretary of State for Scotland appointed him as chairman of the South-Eastern Regional Hospital Board. In this sphere he found a congenial outlet for his energies. He threw himself wholeheartedly into the task of reorganizing the hospital service. In spite of physical handicaps he spared no effort in attending innumerable committee meetings, in visiting all the hospitals in the area, and in getting to know the members of the medical staffs. After a gallant fight against illness he found it necessary to resign from the chairmanship of the Board some few weeks ago.

Jim Greenlees lived a full, a strenuous, and a happy life. To meet him was a stimulating experience, to know him a rare privilege.

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Dr. SOPHIA GRAHAM (née Antonovitch), who died on May 8 at the age of 49, came to this country from Yugoslavia to study medicine in 1922. At the close of the first world war medical women were unknown in the newly constituted State of Yugoslavia, and there were no facilities for medical education: the male practitioners had all been trained in the old Austrian Empire. The British Women's Medical Mission that operated in the old Serbia under the leadership of Sir James and Lady Berry sought to remedy this by arranging for the training of a promising girl in this country in the hope that she would be able ultimately to interest her fellow countrymen in female medical education. Sophia Antonovitch, then in her nineteenth year, was recommended for the first scholarship and brought to England to train at the Royal Free Hospital. Her career as a student was brilliant: she very quickly acquired an intimate knowledge of English and distinguished herself at the medical school in physiology and allied subjects. She graduated M.B., B.S.(London) in 1928. Her devotion to the laboratory had early marked her as a potential research worker, and when she had taken her degree she decided to devote some years to research at the outset of her career. She was most particularly interested in the study of what is now known as psychosomatic medicine, and she naturally gravitated to the Central Pathological Laboratory of the L.C.C. mental hospitals' department at the Maudsley Hospital. After a period as a grant-aided research worker she joined the laboratory staff—she had taken the D.P.M. in 1932. The debt that the laboratory owed to her efforts was so generally acknowledged that when she married Dr. John Graham in 1935, by a unique exception to the rule requiring women to resign on marriage, she was allowed to continue at her post. She retired in 1939 to assist her husband in his practice.

F. L. G. writes: Dr. Sophia Graham's enthusiasm was unbounded and her dexterity and resourcefulness as a laboratory worker were generally recognized. She contributed to a number of researches, and her work on the bodily concomitants to mental imagery will undoubtedly bear fruit when psychologists can be induced to pay attention to contributions from the physiological laboratory. She was a woman of very wide culture and keenly interested in many activities outside her profession. For the past year she faced with courage a long and painful malady from which she well knew there is in the present state of knowledge no hope of recovery.

Surgeon Rear-Admiral JOHN SCARBROUGH DUDDING, who died at Winteringham, Lincs, on May 12 at the age of 73, served in the Royal Navy for 35 years and was appointed an honorary physician to the King in 1935. He was born at Garthorpe, Lincs, in 1877, and went to Oundle School. At the London Hospital he was Buxton Scholar and qualified in 1900, entering the Royal Navy as a surgeon in the same year. He was promoted to staff surgeon in 1908, to surgeon commander in 1916, to surgeon captain in 1926, and to surgeon rear-admiral in 1932. While serving in H.M.S. *Lancaster* he rendered good service at the Messina earthquake in 1909, and received from the Italian Government the Order of Officer of St. Maurice and St. Lazzore. In 1929 he was appointed director of medical studies at the R.N. Medical School, and in 1933 he became medical officer in charge, R.N. Hospital, Plymouth. He served in that post for three years, and was then placed on the retired list at his own request in order to facilitate the promotion of junior officers. He was appointed O.B.E. in 1925 and C.B. in 1935.

# Medico-Legal

## FATAL HYPERSENSITIVITY TO PENICILLIN

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The first recorded case in Great Britain of death due to hypersensitivity to penicillin was investigated by the Newport District Coroner on April 27 at the inquest on a baby girl. She had died after penicillin treatment for superficial burns. It was said that only five similar cases had ever been recorded, all in America.

On March 16, Jane Patricia Simonds, a healthy child aged 14 months, was burned on the left side of her head and face and on her left hand by spilt frying fat. Her mother at once took her to the Royal Gwent Hospital. She was seen by the casualty officer, who found a first-degree burn involving an area of about 4 in. by 3 in. (10 × 7.6 cm.) on the left side of her head extending on to her face. Her temperature and pulse were normal, she was not suffering from shock, she had no rash, and her general condition was good. The burn was dressed, she was given penicillin treatment, and sent home, and her mother was told to bring her to hospital next morning for dressing. Next day she was accordingly seen again by the casualty officer, who found her condition unchanged, and the burn was again dressed.

On that evening a doctor was called to the child's home because of swelling round her eyes. As she was not hot and had no rash he did not think it advisable to send her to hospital immediately. She was worse next morning, and when taken to hospital for dressing was at once admitted because of swelling of the face near the burnt surface. This appeared to respond to treatment, but on the evening of the next day, March 19, her temperature rose to 103° F. (39.4° C.), and on the following day a rash appeared and her temperature continued to rise. She died at 11.30 p.m. on March 21, five days after the penicillin treatment was first given.

At the post-mortem examination carried out next day it was found that the burnt area was clean and was healing, and the brain was normal. The whole body was covered with a diffuse rash. On opening the chest a quantity of clear yellow fluid gushed out. In each pleural cavity 10–15 oz. (284–426 ml.) of fluid was present, and the lungs were oedematous and somewhat collapsed. The heart was normal, but it was contracted and all the chambers were empty; there was an effusion of about 6 oz. (170 ml.) of clear yellow fluid in the pericardial cavity, which was under tension. Spleen and liver were firm and normal, as were the kidneys, apart from congestion of the medulla and ischaemia of the cortex. The adrenals were congested. The stomach and intestines were distended with gas, and there was an effusion of clear fluid into the peritoneal cavity.

In the opinion of Mr. R. V. Jones, who carried out the necropsy, death was caused by cardiac failure due to embarrassment of the heart's action by the pressure of the fluid in the pericardium. This was part of a general out-pouring of fluid into the serous cavities of the body which is typical of a sensitivity reaction. The rash and constriction of the smooth muscle of the intestinal sphincters were evidence in support of such a reaction. There was no evidence that any extraneous substance had gained access or that the reaction was caused by the breakdown of the tissue substances in the burnt area, which was clean and healthy. On laboratory examination the fluid effusions showed no micro-organisms and no characteristics of inflammatory exudates. Mr. Jones concluded that since penicillin was the main agent used in treating the burn it was probably penicillin which had caused the sensitivity reaction. Although mild reactions to penicillin such as rashes, pyrexia, and joint effusions had been recorded, he had been able to find no previous record of a fatal reaction.

The coroner recorded the cause of death as cardiac tamponade due to hypersensitivity reaction to penicillin.

# Universities and Colleges

## UNIVERSITY OF OXFORD

Provided a suitable candidate presents himself the Board of the Faculty of Medicine intends to appoint a Betty Brookes Research Fellow, who will be expected to devote himself to a study of brain metabolism in relation to nervous and mental disease. The Fellowship is tenable for three years in the first instance, but a Fellow is re-eligible, and the stipend will be not more than £1,200 per annum. It is not essential that a candidate should have medical qualifications. Applications must reach the Whitley Professor of Biochemistry, University Museum, Oxford, by June 30.

## UNIVERSITY OF CAMBRIDGE

The Council of the Senate has gratefully accepted the offer of the Trustees of the Nuffield Foundation to renew for a third period of three years its grant of £6,000 a year for an investigation under the direction of Sir Frederic Bartlett, F.R.S., into the causes and results of ageing.

In Congregation on May 12 the degree of M.A. was conferred on Dr. R. A. Noble, Associate Lecturer in the Faculty of Medicine. The degrees of M.B., B.Chir. were also conferred on B. E. L. Thompson.

Dr. Alfred Tissières has been elected into a Fellowship of King's College, Cambridge.

## UNIVERSITY OF EDINBURGH

Professor Warren H. Cole, Professor of Surgery in the University of Illinois, will deliver a Macarthur Postgraduate Lecture in the surgery lecture theatre, University New Buildings, Edinburgh, on Friday, June 15, at 5 p.m. His subject is "Electrolyte Imbalance in Surgery." Senior students and graduates in medicine are invited to attend the lecture.

## UNIVERSITY OF DURHAM

Professor Warren H. Cole, Professor of Surgery in the University of Illinois, will deliver a lecture on "Carcinoma of the Stomach" at the Royal Victoria Infirmary, Newcastle-upon-Tyne, on Thursday, June 14, at 5.15 p.m.

## UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part I:* E. F. Carr, A. A. Cashmore, G. F. Vaughan.

THIRD M.B., B.S.—[1 4]G. A. E. Baker, [1 3]Agnes R. D. Bartels, [1 7]Elaine M. Belton, [1 4 6]A. M. Dawson, [1 7]A. E. Dormer, [1 6]A. Gillespie [1 3 7]N. A. J. Hamer, [1 6]Marion J. P. Jenkins, [1 5]Zilla M. Kaye, [1 6]R. C. Lewis, [1 3]Cicely J. Millbank, [1 6]J. W. Mold, [1 5]M. A. Pears, [1 5]A. Singer, [1 6]M. Sutton, [1 6]A. W. Tranter, [1 3]Coral I. Welch, K. R. Aberdour, J. F. Adam, J. A. M. Ager, Valerie M. D. Alcock, J. H. Allison, B. Altman, D. B. Amos, R. D. Andrews, J. M. Angeloni, R. A. J. Anthony, G. H. Apthorp, Joyce A. Arscott, J. H. Bailey, Helen J. Barnes, A. P. Barter, P. J. Batchelor, P. R. Bateson, Elizabeth L. Batson, C. H. Bearblock, J. Beasley, T. R. Beatson, T. G. L. Bellis, J. Bendas, F. W. Best, G. Birch, R. L. Bird, B. Ll. Bisley, O. H. Blacklay, J. A. Blundell, G. P. B. Boissard, F. E. Bonner, Pauline M. Bousquet, Audrey A. Boutwood, P. R. W. Boyd, A. L. C. A. M. Bracchi, Catherine M. Bradford, P. W. W. Branch, A. R. Brighten, B. St. J. Brown, P. P. Brown, W. Brumfitt, T. A. Bryant, A. F. Buck, P. E. Burden, D. M. Burley, J. A. B. Burn, C. F. Caldwell, J. C. D. Callander, J. C. Camac, L. Candiah, M. J. Cassells, H. N. Chambers, P. A. Chapman, V. R. Chuck, J. D. Clark, G. Clementson, L. F. Cleveland, W. G. Cleverly, D. J. Cliffe, G. E. Clulow, J. B. Coldrey, P. A. Coldrey, D. J. Coleman, M. K. Coles, Daphne C. Collins, H. W. M. Collymore, P. H. Connell, E. N. Coomes, M. P. M. Cooray, J. L. M. Corbet, J. C. Cornwell, Delia M. H. H. Cothay, P. H. E. Courtenay, F. J. Covill, A. N. Cowan, C. W. Crane, J. M. D. Crook, A. F. Cross, J. V. Dadswell, Mary D. Daly, Audrey Davidson, Joan R. Davies, J. P. H. Davies, J. P. Davies, D. M. Devane, D. G. Dick, A. B. Dickie, J. C. Dilley, G. Dixon, J. W. Dodson, J. A. Dossett, J. M. Doyle, Marie Driver, M. V. Driver, R. D. P. Druitt, R. J. Drysdale-Anderson, Barbara Duguid, F. M. Dunn, C. E. Durber, G. W. Edward, S. C. Emerick, R. Emery, Beatrice M. Evans, T. W. Evans, A. C. Fairburn, S. T. Faithfull, J. D. Farley, C. P. Finch, Kathleen T. Flanagan, P. T. Flute, D. L. Foote, R. H. Fox, S. Freier, J. H. Fryer, A. P. Fuller, D. H. Gamage, K. M. Gammie, N. H. Gelpke, A. A. Gibberd, Hilda L. Gibbs, P. R. Gilbert, A. L. A. Gill, J. W. Goodfellow,

M. H. Gough, G. T. Gould, G. F. Grave, Pamela E. Green, D. Greenbaum, Joan Greene, Brenda Griffin, G. T. Griffith, Mary P. Gummer, B. C. Hale, M. H. Hambling, J. W. Hamlett, D. J. Handford, D. H. C. Harland, P. Harnarayan, W. R. Harrison, Robina Harry, C. J. R. Hart, Helena J. Harthoorn, M. D. A. Heller, N. G. B. Hersey, A. J. Hibell, A. C. Hill, R. C. Hobbs, D. C. Hodgson, B. W. Holbrook, G. C. A. Holden, J. M. Holden, J. M. Hood, I. A. Horton, H. V. Hoyle, Penelope C. Humphries, C. P. Hunt, Olive Ibberson, R. N. Ibbotson, D. Jackson, J. H. M. James, W. V. James, R. J. Jameson, G. H. Jantet, J. V. Jeffs, Pamela Jewell, A. H. John, K. Jones, R. F. Jones, T. R. Jones, M. J. Keith, T. D. Kellaway, J. C. C. Kendall, P. H. Kendall, P. J. Koblenzer, Mary I. Legg, A. G. Leslie-Smith, D. C. Levin, D. M. Lewis, J. G. Lewis, M. Lewis, J. S. Lowry, Colina C. Mackenzie, K. E. MacLachlan, K. L. McNeilly, J. G. Mander, J. W. Mann, G. E. Manning, E. J. Masters, Frances E. Mather, J. R. M. Mathieson, Althea G. Matthews, Margaret B. Mearns, J. M. Medlock, A. J. Merrifield, R. P. Michael, P. McK. Middleton, Anne E. Millar, Margery L. Moncrieff, J. L. Montagnon, J. Moran, Avisa J. M. Morley, M. C. T. Morrison, W. H. Mortiboys, R. F. Mottram, J. S. Mousley, F. J. Moynihan, A. Muir, Shirley E. Nathan, R. C. Nauth-Misir, Marianna Newman, A. J. Newton, J. G. Nicholson, P. J. Nobes, J. P. Norman, K. R. Norton, M. J. C. O'Brien, P. M. J. O'Brien, T. M. O'Brien, D. R. M. P. B. O'Sullivan, J. N. Pachmayr, S. A. C. Paget, J. Palmer, J. A. Parrish, J. W. B. Parsons, R. E. H. Partridge, Jacqueline S. Pennycuick, A. G. Penrose, R. J. Pett, A. R. Phillips, G. A. Phillips, H. O. Phillipson, J. C. Pittman, T. A. Plumley, J. C. Pollard, Ariela Pomerance, J. C. Pond, J. M. Powley, I. G. Pryce, W. J. Pryn, Barbara R. Purchas, J. A. Rassell, C. H. R. Read, J. D. Redmill, S. H. Richards, R. A. A. Rickett, F. Ll. Roberts, J. McK. N. Roberts, R. E. Ll. Roberts, B. F. Robinson, G. E. Robinson, Ruth M. Robinson, A. Robson, D. A. Roche, A. Rodger, Margaret Rooms, I. Rosen, D. L. Rugg-Easey, D. H. Rushton, P. S. B. Russell, J. A. Rycroft, G C. Saint, J. R. Saunders, H. M. Saxton, I. P. Q. Scott, R. Sepson, C. H. Sheridan, S. Shuster, D. D. Silver, S. C. Simmons, A. J. Sims, H. P. Smith, K. G. Smith, K. J. Southgate, Constance R. Spittle, A. G. Spooner, Joan V. Stavert, V. L. Steinberg, R. V. Steward, D. Stewart, D. J. Stoker, T. Sussman, E. P. W Tatford, C. W. Taylor, J. Taylor, W. N. A. Taylor, J. Terry, I. B. Thomas, T. G. Thomas, J. A. Thornton, A. C. Trevan, W. M E. Tweed, V. Udall, P. Venables, R. J. Venn, Edith Wahl, A. H. Walker, G. F. Walker, J. D. Walters, P. J. R. Walters, D. M. Warner, M. A. T. Waters, M. G. Webber, C. P. Wendell Smith, E. D. West, W. T. White, A. E. Wilkinson, B. R. Wilkinson, D. K. Williams, J. F. Williams, P. J. Williamson, F. Wilson, D. Wimborne, J. Winstanley, Vivienne L. L. Wolfson, L. Wollner, C. H. Wood, P. R. T. Wood, R. Woodside, K. G. Worms, E. H. Wyatt, H. J. Wyatt, M. D. Youings, J. V. I. Young, Joan F. Zilva.

[1]With honours. [2]Distinguished in Pathology. [3]Distinguished in hygiene and forensic medicine. [4]Distinguished in medicine. [5]Distinguished in applied pharmacology and therapeutics. [6]Distinguished in surgery. [7]Distinguished in obstetrics and gynaecology.

The following candidates have been approved at the examination indicated:

POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—D. Anton-Stephens, K. Bobath, R. B. Carr, M. B. Contractor, W. A. Cramond, H. W. D. Davies, J. Denham, L. H. Field, G. F. J. Goddard, E. S. Goller, Herta Graz, B. A. J. C. Gregory, L. G. W. J. Hannah, Mercy I. Heatley, D. Irwin, M. A. Jackson, W. G. Joffe, J. C. Kerridge, Hazel W. Liddell, J. S. B. Lindsay, J. S. Pippard, E. Roderic-Evans, P. D. W. Shepherd, S. Smith, G. F. Spaul, S. J. G. Spencer, H. P. Tarnesby, E. L. Udwin, A. A. Valentine (with Mental Deficiency in Part B), K. R. H. Wardrop, Letitia E. Woodvine. All with Mental Diseases (Psychiatry) in Part B, unless otherwise shown. *Part A:* E. Benjacar, D. H. Bennett, C. Borg, J. H. Brown, Nina A. Cohen, J. D. C. Currie, G. A. Dransfield, B. V. Earle, M. M. Ernst, M. H. Friedman, G. P. Hartigan, J. A. Irwin, N. B. Jetmalani, K. S. Jones, I. S. Kreeger, N. P. Lancaster, R. C. MacGillivray, E. Marley, W. Pappenheim, J. M. K. Rehmany, E. J. Rich, W. D. G. Robson, W. F. Salter, R. C. Simpson, R. W. Simpson, Daphne G. D. T. Smedberg, R. A. Y. Stewart, G. E. Swinney, W. B. Tudor, E. A. Williams, S. C. B. Yorke.

Peter Brian Medawar, D.Sc., F.R.S., has been appointed to the Jodrell Chair of Zoology and Comparative Anatomy, tenable at University College, from October 1. Professor Medawar is at present Mason Professor of Zoology in the University of Birmingham and Dean of the Faculty of Science.

Harry Butler, M.D., has been appointed to the University Readership in Anatomy tenable at St. Bartholomew's Hospital Medical College, from October 1.

### UNIVERSITY OF MANCHESTER

Dr. Colin Fraser Brockington has been appointed Professor of Social and Preventive Medicine in the University in succession to Professor Andrew Topping and will take up his duties in August. Dr. Fraser Brockington qualified M.R.C.S., L.R.C.P. in 1927 and took the D.P.H. in the following year. He graduated B.Chir. in 1930, and two years later he obtained the Cambridge M.D. He was appointed Deputy Medical Officer of Health for Warwickshire in 1938 and became the County Medical Officer of Health in 1942. He received his present appointment of County Medical Officer of Health for the West Riding of Yorkshire in 1946 and has been Lecturer in Preventive Medicine in the University of Leeds since 1948.

### UNIVERSITY OF BIRMINGHAM

The following have been appointed representatives of the University: Professor A. P. Thomson on the General Medical Council, in place of the late Sir Leonard Parsons; Professor C. F. V. Smout on the Board of Governors of the United Birmingham Hospitals in place of Professor Hilda Lloyd; and Professor J. M. Smellie on the Standing Joint Committee of the University, the United Birmingham Hospitals, and the regional hospital board in place of Professor Hilda Lloyd.

The following have been appointed University Clinical Lecturers from April 1: Dr. L. Nagley (Medicine); Mr. A. B. Watson (Surgery); Mr. E. A. Turner (Neurosurgery); Mr. R. Evans (Diseases of Ear, Nose, and Throat); and Dr. J. W. Woodward (Anaesthetics).

Dr. B. S. B. Wood, Lecturer in Paediatrics, has resigned his appointment on becoming Assistant Paediatrician at the Dudley Road Hospital.

### UNIVERSITY OF LIVERPOOL

Dr. Andrew Wilson, Reader in Applied Pharmacology at University College, London, has been appointed to the Chair of Pharmacology in the University of Liverpool.

### UNIVERSITY OF LEEDS

Dr. A. B. Eastwood has been appointed Lecturer in Anaesthetics and Dr. T. H. Flewett Lecturer in Bacteriology.

### UNIVERSITY OF SHEFFIELD

The title of Reader in Pathology has been conferred on Dr. H. E. Harding, at present Senior Lecturer in Pathology.

Dr. D. M. Matthews has been appointed Honorary Demonstrator (part-time) in Physiology.

Dr. A. A. Belton, Dr. E. J. Clegg, Dr. J. A. Howarth, and Dr. P. A. King have resigned their appointments as demonstrators in anatomy on returning to clinical work, and Mr. T. Smith has resigned his appointment as temporary lecturer in obstetrics and gynaecology on becoming Consultant in Obstetrics and Gynaecology to the Northern Regional Hospital Board.

## The Services

A *Supplement* to the *London Gazette* has announced the following awards:

*Three Clasps to the Territorial Efficiency Decoration.*—Major R. H. Mortis, T.D., R.A.M.C.

*Two Clasps to the Territorial Efficiency Decoration.*—Colonel J. B. S. Guy, C.B.E., T.D., and Majors F. J. L. Lang, T.D., and J. M. Lees, T.D., R.A.M.C.

*First Clasp to the Territorial Efficiency Decoration.*—Lieutenant-Colonels H. D. Chalke, O.B.E., T.D., and C. K. Sconce, T.D., Major (acting Lieutenant-Colonel) W. H. Wolstenholme, O.B.E., T.D., Majors D. S. Austin, T.D., J. G. McDowell, T.D., and F. E. Street, T.D., R.A.M.C.

*Territorial Efficiency Decoration and First Clasp.*—Lieutenant-Colonel (acting Colonel) D. H. Young, Lieutenant-Colonels A. Barber, M.C., C. Berens, A. T. Burn, R. P. Kemp, A. McQuiston, and G. C. Pether, Major (acting Colonel) P. Hawe, Majors (Honorary Lieutenant-Colonels) R. Evans, O.B.E., C. E. Moorhead, O.B.E., and H. B. Porteous, Majors R. W. Evans, J. L. Fraser, J. R. Hamerton, and E. Shipman, and Captain F. Buchan, R.A.M.C.

*Territorial Efficiency Decoration.* — Lieutenant-Colonels R. G. W. Ollerenshaw, A. B. Pain, and T. D. Pratt, Honorary Lieutenant-Colonel F. B. Mackenzie, D.S.O., M.C., T.D., retired, Majors E. V. Bevan, A. B. Dick, and A. K. Dougall, M.C., and Captains (Honorary Majors) S. R. A. Beckett, G. F. Petty, and J. A. W. Shearer, R.A.M.C.

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles for the week ending May 12 (No. 19).

Figures of notified *cases* are for: (*a*) England and Wales (London included). (*b*) London (administrative county). (*c*) Scotland. (*d*) Northern Ireland. (*e*) Eire. Figures of *births and deaths* and of *deaths* recorded under each disease are for: (*a*) The 126 great towns in England and Wales (London included). (*b*) London (administrative county). (*c*) The 16 principal towns in Scotland. (*d*) The 10 principal towns in Northern Ireland. (*e*) The 13 principal towns in Eire. A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, Northern Ireland, and Eire, the Ministry of Health and Local Government of Northern Ireland, and the Department of Health of Eire.

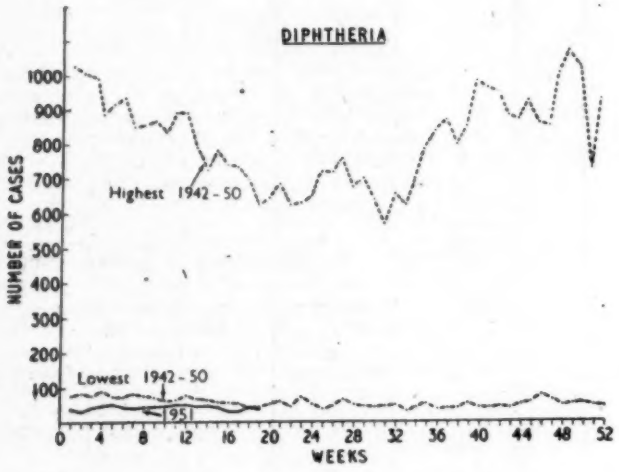
| Disease | 1951 Week Ending May 12 | | | | | 1950 Corresponding Week | | | | | 1942–50 England & Wales Corresponding Week | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | (*a*) | (*b*) | (*c*) | (*d*) | (*e*) | Highest | Median | Lowest |
| Diphtheria | 38 | 3 | 18 | 1 | — | 43 | 2 | 12 | 3 | 2 | 629 | 368 | 43 |
| Deaths | — | — | — | — | — | — | — | — | — | — | | | |
| Dysentery | 940 | 196 | 151 | 19 | 3 | 444 | 15 | 103 | 1 | 3 | 444 | 111 | 77 |
| Deaths | | — | | — | | | | | — | | | | |
| Encephalitis, acute | 2 | — | — | — | | 3 | — | — | — | | 10 | 3 | — |
| Deaths | | — | | | — | | — | | | — | | | |
| Erysipelas | | | 23 | 2 | 3 | | | 22 | 7 | 9 | | | |
| Food-poisoning | 107 | 11 | | — | | 54 | 9 | | 8 | | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 17 | 22 | | | | | 20 | | | |
| Deaths | 6 | | 2 | 2 | 2 | 17 | | 6 | — | 1 | | | |
| Measles* | 19,929 | 881 | 494 | 284 | 182 | 7,278 | 262 | 656 | 260 | 209 | 12,412 | 8,149 | 2,132 |
| Deaths | | 1 | — | — | 1 | | | 2 | 1 | — | | | |
| Meningococcal infection | 33 | 2 | 24 | — | | 37 | 5 | 28 | — | 1 | 168 | 59 | 36 |
| Deaths | | — | — | | | | — | — | | | | | |
| Ophthalmia neonatorum | 32 | 4 | 7 | — | | 31 | 3 | 9 | — | | 78 | 73 | 31 |
| Pneumonia, influenzal | 574 | 36 | 5 | 8 | 1 | 502 | 12 | 7 | 7 | — | 1,095 | 561 | 406 |
| Deaths (from influenza)† | 15 | 3 | — | — | 1 | 17 | 2 | 1 | — | 3 | | | |
| Pneumonia, primary | | | 164 | | | | | 190 | | | | | |
| Deaths | 180 | 36 | | 4 | 6 | 169 | 26 | | 5 | 15 | | | |
| Poliomyelitis, acute: | | | | | | | | | | | | | |
| Paralytic | 11 | 1 | 1 | 1 | 1 | 22 | 1 | 5 | 5 | 2 | 22 | 12 | 2 |
| Non-paralytic | 10 | — | | | | | | | | | | | |
| Deaths§ | 2 | — | | | — | 2 | — | | | — | | | |
| Puerperal fever | | | 2 | | | | — | 7 | | | | | |
| Puerperal pyrexia‖ | 78 | 10 | 6 | — | 1 | 80 | 3 | 11 | 2 | | 169 | 126 | 78 |
| Scarlet fever | 1,025 | 66 | 129 | 30 | 57 | 1,322 | 98 | 168 | 80 | 83 | 1,791 | 1,322 | 993 |
| Deaths | | — | — | — | — | | | — | — | — | | | |
| Smallpox | — | — | — | — | | — | — | — | — | | | | |
| Deaths | | | | — | | | | | — | | | | |
| (1) Tuberculosis, respiratory | | | 202 | 46 | | | | 198 | 37 | | | | |
| (2) Tuberculosis, non-respiratory | | | 33 | 4 | | | | 46 | 8 | | | | |
| (1) Deaths | 138 | 24 | 19 | 7 | 12 | 178 | 23 | 29 | 2 | 7 | | | |
| (2) Deaths | | 3 | 7 | 4 | 3 | | 5 | 9 | 1 | 2 | | | |
| Typhoid fever | 3 | 1 | — | — | 2 | 6 | — | — | 1 | 4 | | | |
| Deaths¶ | — | — | — | — | | — | — | — | — | | 25 | 13 | 7 |
| Paratyphoid fever | 10 | — | — | — | | 11 | — | — | — | | | | |
| Whooping-cough | 3,206 | 161 | 469 | 48 | 51 | 3,469 | 203 | 386 | 59 | 131 | 3,469 | 2,222 | 799 |
| Deaths | 7 | 1 | — | — | — | 2 | 1 | — | — | — | | | |
| Deaths (0–1 year) | 227 | 33 | 37 | 8 | 19 | 249 | 33 | 36 | 13 | 19 | 435 | 341 | 249 |
| Deaths (excluding stillbirths) | 4,835 | 794 | 587 | 111 | 174 | 4,757 | 754 | 588 | 123 | 168 | 4,776 | 4,529 | 4,290 |
| Annual death rate (per 1,000 persons living) | | | 11·9 | | | | | 11·8 | | | | | |
| Live births | 7,721 | 1,272 | 989 | 233 | 412 | 7,875 | 1,282 | 999 | 246 | 366 | 10,108 | 7,886 | 5,833 |
| Annual rate per 1,000 persons living | | | 20·0 | | | | | 20·1 | | | | | |
| Stillbirths | 188 | 24 | 24 | | | 200 | 23 | 21 | | | 277 | 216 | 171 |
| Rate per 1,000 total births (including stillborn) | | | 24 | | | | | 21 | | | | | |

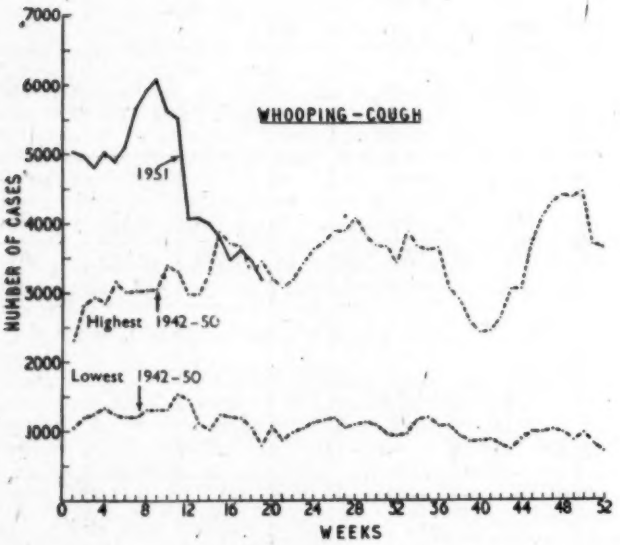
* Measles not notifiable in Scotland and returns are approximate. † Includes primary form for England and Wales, London, and N. Ireland. § The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, and London (administrative county), are combined. ‖ Includes puerperal fever for England and Wales and for Eire. ¶ Deaths from paratyphoid fever are combined with those from typhoid fever.

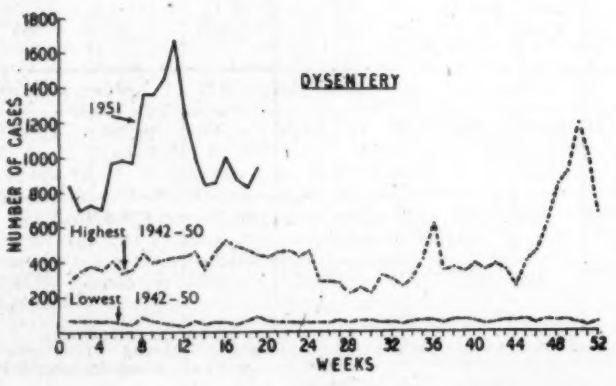
# Vital Statistics

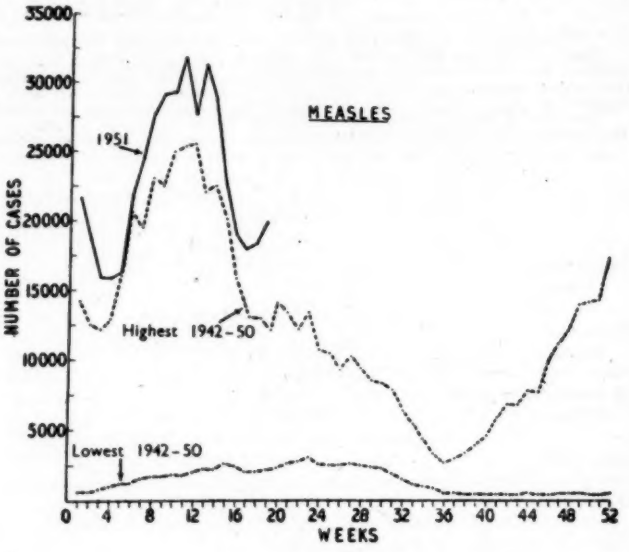
## Graphs of Infectious Diseases

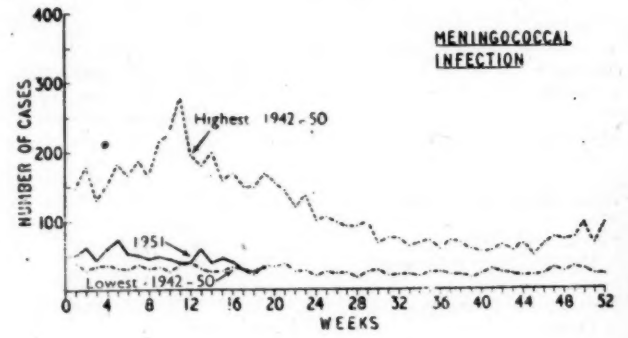
The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported during the nine years 1942–50 are shown thus - - - - - - -, the figures for 1951 thus ———. Except for the curves showing notifications in 1951, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.

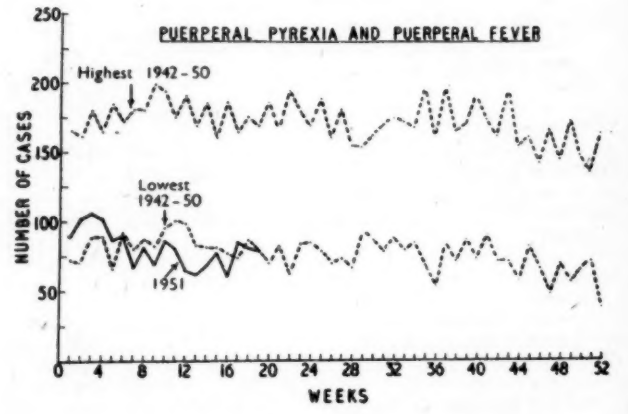



## Infectious Diseases

The chief variations in the trends of infectious diseases in England and Wales during the week ending May 12 were increases in the number of notifications of measles 1,619 and dysentery 107 and a decrease of 277 for whooping-cough.

A rise in the incidence of measles was recorded in every region with the exceptions of Yorkshire and the north-west. The largest increases in the number of notifications were in Northumberland 266, Kent 194, Derbyshire 183, Devonshire 155, and the chief exceptions to the rising trend were decreases in Yorkshire West Riding 255 and Southampton 165. No change of any size occurred in the local trends of scarlet fever. The largest falls in the number of notifications of whooping-cough were Lancashire 71 and London 57, while the largest rise was 59 in Warwickshire. No changes were recorded in the trends of diphtheria; the largest return was Lancashire 9 (Manchester C.B. 5). The number of notifications of acute poliomyelitis was the

same as in the preceding week (21). Two cases of acute poliomyelitis were notified in each of the cities of Birmingham, Coventry, and Manchester.

The higher incidence of dysentery was due to rises in established outbreaks, and no fresh outbreak of any size was reported during the week. The largest returns of dysentery were London 196 (Islington 44), Lancashire 192 (Manchester C.B. 26, Oldham C.B. 21), Yorkshire West Riding 77 (Skipton U.D. 26, Bradford C.B. 20), Middlesex 72 (Edmonton M.B. 18, Ealing M.B. 17).

### World Population

The growth of the world's population between 1920 and 1949 is discussed in the *Demographic Yearbook, 1949–50*, issued by the United Nations. Some statistics of population are admitted to be unreliable, especially in Africa and many parts of Asia, but if the figures are accepted as a rough approximation they will not be entirely misleading.

The population of the world increased from 1,834 million in 1920 to 2,378 million in 1949. That is an increase of 30% on the 1920 figure and corresponds to an increase of slightly less than 1% per annum. If this rate of growth is maintained, the present world population will be doubled in less than 100 years. The greatest increase was in Latin America, the reliability of whose estimates is described as "fair." In 1920 the population was 92 million and in 1949 it was 158 million—an increase of 72%. The smallest increase was in North-west-central Europe, the reliability of whose estimates is described as "good." Here there was a 19.5% increase from 179 million in 1920 to 214 million in 1949. The population of Eastern Europe, including the Asiatic parts of the U.S.S.R., increased by 22% from the 1920 figure of 236 million to the 1949 figure of 288 million ("fair" reliability). The United States and Canada, whose estimates are reliable, had a population increase of 42% from 115 million in 1920 to 163 million in 1949. Smaller than the increase found in Latin America, and larger than that found in the United States and Canada, was the increase in the population of Japan, whose estimates are also reliable; it rose from 56 million in 1920 to 83 million in 1949—an increase of 48%.

Japan is by far the most densely populated region in the world, having in 1949 223 persons per square kilometre. The next most densely populated is South-central Asia with 100 per square kilometre. The comparable figure for North-west-central Europe was 78, for Southern Europe 88, for Eastern Europe including the Asiatic part of the U.S.S.R. 12, for the United States and Canada 8, and for Latin America 8.

### Births and Deaths in the U.S.A.

In 1950 in the U.S.A. the crude birth rate was 23.5 per 1,000 population, as compared with 24.0 in 1949 and 25.8 in 1947. If an estimate is made of unregistered births, the crude birth rate for 1950 becomes 24.5. The estimated death rate in 1950 was 9.6 per 1,000 population, as compared with 9.7 in 1949. The estimated infant mortality rate was 29.2 per 1,000 live births in 1950—a record low level. It was 31.1 in 1949. (Public Health Service *Monthly Vital Statistics Bulletin*, April 24, 1951.)

### Births and Deaths in Capetown

In the year ending June 30, 1949, the European population of Capetown was 194,085 and the non-European population 219,644 (*Annual Report* of the Medical Officer of Health of the City of Capetown). Some birth and death rates are shown in the following Table:

| | European | Non-European |
|---|---|---|
| Birth rate .. .. .. .. | 19·23 | 46·13 |
| Death rate .. .. .. .. | 9·10 | 18·13 |
| Infant mortality rate .. .. | 29·29 | 110·88 |
| Tuberculosis death rate* .. | 0·42 | 4·89 |

* Per thousand population.

### Week Ending May 19

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 991, whooping-cough 2,556, diphtheria 31, measles 18,381, acute pneumonia 483, acute poliomyelitis 24, dysentery 661, paratyphoid fever 10, typhoid fever 6. Deaths from influenza in the great towns numbered 8.

# Medical News

### What W.H.O. is Doing

The fourth W.H.O. Assembly ended at Geneva on Friday, May 25, after taking a number of decisions, the most important of which was probably the unanimous adoption of the international sanitary code, which prescribes maximum as well as minimum regulations and therefore should prevent the imposition by any country of special health regulations purely for reasons of commerce or prestige. An effective working budget of $7,677,782 was approved for the coming year, and the U.S. contribution adjusted to be one-third of this total (it has hitherto been greater); the subscriptions from Austria and from Japan (now admitted a member of W.H.O., together with Spain and the Federal German Republic) were modified to follow changes in political status. It was decided to maintain the Tuberculosis Research Office in Copenhagen, subject to biennial review, and the agreement between W.H.O. and the Egyptian Government on the diplomatic status of the staff of the Regional Office in Alexandria was approved. The application of the International Catholic Committee of Nurses and Medical Social Workers for admission into official relationship with W.H.O. was opposed on many sides, and a resolution for postponement of the application was passed by 27 to 9, with 15 abstentions.

### Harveian Society of London

The Buckston Browne dinner was held at the Hyde Park Hotel on May 10 with the President, Mr. W. E. Tucker, in the chair. The Rt. Hon. L. S. Amery proposed the health of the society; in a wise and witty speech he referred to the Harveian concept of man's function. The president, in his reply, appealed for a continuance of unity and friendship in the medical profession. Dr. Brian Warren, who proposed the health of the guests, told of several interesting aspects of Stuart history as seen through the eyes of William Harvey. Replies were made by Sir Alexander Maxwell (chairman of University College Hospital), who delighted the company by his sparkling humour, and by Mr. Basil Cameron, who made a graceful speech of thanks.

### Ulster Paediatric Society Dinner

The Ulster Paediatric Society held a dinner on May 18 at Ballygally Castle Hotel, Co. Antrim, with Professor F. M. B. Allen in the chair. There was a large attendance of members and guests; the principal guest was Professor A. G. Watkins, Welsh National School of Medicine, who gave an address on "Acute Respiratory Obstruction in Children."

### British Cardiac Society

The thirteenth annual general meeting of the British Cardiac Society was held in Glasgow on May 10 under the chairmanship of Dr. J. H. Wright. At the morning session there was a discussion on heart disorders of pulmonary origin, the opening speakers being Professor J. McMichael, Dr. A. J. Thomas, and Dr. Paul Wood. In the afternoon short communications, arranged by the secretary, Dr. K. Shirley Smith, included papers on vector cardiography, clinical and cardiographic aspects of cardiac infarction, and electrokymography; colour films illustrating movements of the valves of the heart and diaphragmatic flutter were shown.

### Society of Medical Officers of Health

The following have been elected officers for the session 1951–2. President: Dr. W. G. Clark, medical officer of health, City of Edinburgh. Vice-presidents: Professor R. H. Parry, M.O.H., Bristol), Dr. H. C. Maurice Williams (M.O.H., Southampton), and Dr. J. M. Gibson (M.O.H., Huddersfield). Chairman of council: Sir Allen Daley. Honorary treasurer: Dr. James Fenton. Dr. Clark is the first M.O.H. for Edinburgh to hold this office since the foundation of the society in 1856. Sir Allen Daley has been re-elected as chairman of the council for the fourth year in succession.

### Jacques Arsène d'Arsonval

June 8 marks the centenary of the birth of Professor Jacques Arsène d'Arsonval (1851–1941), famous for his introduction of diathermy and various biophysical researches. The son of a country doctor, he showed much talent for mathematics and physics, and was always interested in the more exact and mathematical aspects of medicine. While a medical student he attended lectures given by the physiologist Claude Bernard; once the galvanometer he used did not work and d'Arsonval repaired it for him. Bernard offered him an assistantship in his research laboratory, and d'Arsonval devoted himself to studying and experimental work in physiology, at the same time continuing his medical studies. He received his doctorate when he was 26 for a thesis on pulmonary elasticity. In 1882 he became director of the biophysical laboratory of the Collège de France, and subsequently professor. His researches covered a wide field—from the invention of numerous electrical instruments to the study of high-frequency currents and their physiological effects, and the heat production of fishes.

### Julius Leopold Pagel (1851–1912)

Born on May 29, 1851, Pagel is known to the medical profession at large through his *Biographisches Lexikon*, while the medical historian values his readable *Geschichte der Medicin*, his *Handbuch*, and his *Zeittafeln*. As a general practitioner, Pagel began lecturing on medical history at the University of Berlin in 1891, being made professor extraordinary in 1901. He died on January 31, 1912. At a meeting of the Osler Club held in his honour at the Wellcome Research Institution on May 4, Dr. Walter Pagel spoke on "Julius Leopold Pagel and the Usefulness of Medical History for Medicine."

### Osler Club and Library

It is not generally known that the Osler Club library was almost completely destroyed during the war, and that efforts are now being made to rebuild the collection. At present it consists merely of a few books and reprints by Sir William Osler, a few biographies devoted to him, and about 2,000 reprints mainly devoted to the history of medicine. Members of the medical profession are invited to send copies of their own books on the history of medicine and to remember the Osler library when disposing of books. A list of the books already owned by the club is available to those wishing to help. The library is at present housed in the Medical College Library, St. Bartholomew's Hospital, E.C.1. The Osler Club now has about 70 members and is open to all members of the medical profession, students, and laymen. The subscription is 15s. a year (10s. for undergraduates), and new members or guests will be welcomed at any time. There is no entrance fee.

### Aureomycin and Chloramphenicol Regulations

From June 1 these two antibiotics will, like penicillin under the Penicillin Act, 1947, be available only from registered pharmacists on prescription. These regulations anticipate the wider availability of aureomycin.

### Helicopters in Korea

General Bliss, Surgeon General to the U.S. Army, has reported that the use of helicopters by the Mobile Army Surgical Hospitals has been most successful in Korea. Each unit has a number of helicopters attached to it; the pilots live with the unit, and when a call comes from the clearing station at the front lines the helicopter can take off immediately. Those now in use in Korea carry two patients strapped in basket-type litters on the outside. A new type is now being tried out; this is a Sikorsky helicopter that can carry eight patients inside it. At present there is only one in operation in Korea.

### Wills

Major-General Robert James Blackham, of Etchingham, Sussex, barrister-at-law, a member of the Pharmaceutical Society of Ireland, author, and a Liveryman of the Society of Apothecaries, who was also a Freeman of the City of London and Under-Sheriff of the City of London, 1935–6, left £1,749, including £100 each to the Royal Institute of Public Health and Hygiene and the Royal Faculty of Physicians and Surgeons of Glasgow, to provide an annual lecture, to be known as the Blackham Lecture.

## COMING EVENTS

### Osler Club Meeting

The next meeting of the Osler Club will be held on June 15, at 7.45 p.m., at the Medical Society of London, 11, Chandos Street, Cavendish Square, W.1, in commemoration of Sir Oliver Lodge (1851–1940). Talks will be given on Sir Oliver by Dr. R. H. Thouless and Mr. W. H. Salter, and Dr. G. F. Newbold will talk on the history of hypnotism.

### Edinburgh Royal Infirmary Residents' Club

The Edinburgh Royal Infirmary Residents' Club is being resuscitated, and the annual dinner is to be held in Edinburgh on June 22. Any member who has not received a notice of this, and who wishes to be present, should write to the honorary secretary, Dr. W. D. A. Callam, 29 Murrayfield Avenue, Edinburgh, 12.

### Tuberculosis Conference

The Oxford Conference on Tuberculosis and Diseases of the Chest will be held from July 16 to 21. It is designed to display British thought and work on these diseases and to stimulate discussion; the sessions will be held in the Taylor Institution and accommodation will be provided in Balliol, St. John's, and Trinity Colleges. Further information may be obtained from the Hon. Sec., Dr. Stephen Hall, 16, Grosvenor Place, London, S.W.1.

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## SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

**Monday**

EDINBURGH UNIVERSITY.—At Physiology Class Room, June 4, 5 p.m., "*The Failure of Systems*," by Dr. Douglas Guthrie.

INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill, London, S.E.—June 4, 5.30 p.m., lecture-demonstration by Dr. E. Stengel.

**Tuesday**

LONDON COUNTY MEDICAL SOCIETY.—At St. Ebba's Hospital, Epsom, June 5, 3 p.m., clinical meeting.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—June 5, 5 p.m., "*Surgery of the Lacrimal Sac and Ducts*," by Mr. T. M. Tyrrell.

ST. MARY'S HOSPITAL MEDICAL SCHOOL: WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, Paddington, London, W.—June 5, 5 p.m., "*Infection and Resistance in Young Animals*," Almroth Wright Lecture by Mr. R. Lovell, D.Sc., M.R.C.V.S.

WEST END HOSPITAL FOR NERVOUS DISEASES, 40, Marylebone Lane, London, W.—June 5, 2.30 p.m., "*Demyelinating Diseases*," clinical demonstration in neurology by Dr. N. G. Hulbert.

### Wednesday

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—June 6, 5 p.m., *"Medical Mycology—Microsporon and Epidermophyton Infections,"* by Dr. R. W. Riddell.

OXFORD UNIVERSITY.—At Radcliffe Infirmary, Oxford, June 6, 5 p.m., *"Gastric Biopsy in the Study of Chronic Gastritis and Pernicious Anaemia,"* Litchfield Lecture by Dr. Ian Wood.

ROYAL EYE HOSPITAL, St. George's Circus, Southwark, London, S.E.—June 6, 5.30 p.m., *"Surgical Treatment of Squint,"* by Mr. R. P. Crick.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., June 6, 7.30 for 8 p.m., annual banquet.

### Thursday

EDINBURGH UNIVERSITY, University New Buildings (Anatomy Theatre), Teviot Place, Edinburgh.—June 7, 5 p.m., *"Infantile Gastro-enteritis,"* Honyman Gillespie Lecture by Dr. Glenys M. Lowdon.

●INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—June 7, 5 p.m., *"Acne Vulgaris and Seborrhoea,"* by Dr. G. B. Mitchell-Heggs.

INSTITUTE OF UROLOGY.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., June 7, 5 p.m., *"Uraemia,"* by Professor M. L. Rosenheim.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—June 7, 5 p.m., *"Uraemia,"* Urology Lecture by Professor M. L. Rosenheim.

ROYAL SOCIETY, Burlington House, Piccadilly, London, W.—June 7, 4.30 p.m., *"Lethal Synthesis,"* Croonian Lecture by Professor R. A. Peters, F.R.S.

ST. ANDREWS UNIVERSITY.—At Lecture Theatre, Materia Medica Department, Medical School, Small's Wynd, Dundee, June 7, 5 p.m., *"Balance of Life and Death in Brain Lesions,"* by Professor Sir Geoffrey Jefferson.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—June 7, 4.30 p.m., *"Neurology,"* lecture-demonstration.

UNIVERSITY COLLEGE: DEPARTMENT OF BIOCHEMISTRY, Physiology Theatre, Gower Street, London, W.C., June 7, 4.45 p.m., *"Biological Syntheses Concerning Carbohydrate Radicles,"* third of four public lectures by D. J. Bell, Ph.D., Sc.D., F.R.I.C.

WESTMINSTER SCHOOL OF MEDICINE, Meyerstein Lecture Theatre, Horseferry Road, London, S.W.—June 7, 5.30 p.m., clinico-pathological demonstration. Discussion: *"A.C.T.H. and Cortisone,"* speakers, Professor N. F. Maclagan, Dr. F. Dudley Hart, and Dr. J. G. Humble.

### Friday

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—June 8, 5.30 p.m., clinical demonstration by Dr. R. T. Brain.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Bedford.**—On May 14, 1951, at Stoke-on-Trent, to Janet (formerly Shrimpton), M.B., B.Ch., wife of Godfrey Thomas Bedford, M.B., Ch.B., D.O.M.S., a son.

**Bunting.**—On May 5, 1951, at 12, Wilmington Road, Quinton, Birmingham, to Vera M., wife of Dr. John Bunting, a daughter—Alison Margaret.

**Crichton.**—On May 20, 1951, at Abyad, Egypt, to Jean, wife of Squadron Leader David Crichton, M.B.E., of Royal Air Force, Kabrit, M.E.A.F., 15, a daughter.

**James.**—On May 15, 1951, at Parkhouse Nursing Home, Liverpool, to Joyce, wife of Dr. H. Watkin James, a son.

**Pillai.**—On April 20, 1951, at Swansea, to Lenora (formerly Anthony), wife of S. Pillai, M.B., F.R.C.S., a son—Mohan Anthony.

### DEATHS

**Carter.**—On May 20, 1951, at his home, Clifford Broadstone, Dorset, William Henry St. Leger Carter, L.R.C.P.&S.Ed., aged 89.

**Connal.**—On May 22, 1951, at the Hospital of St. John and St. Elizabeth, London, N.W., John Connal, M.B., Ch.B., late of Isleworth, Middlesex, aged 59.

**Crean.**—On May 23, 1951, Thomas Francis Crean, O.B.E., L.R.C.P.&S.I., Surgeon Commander, R.N., retired, of 512, Allerton Road, Springwood, Liverpool.

**Gray.**—On May 25, 1951, at Highgate, London, N., Cyril Gray, L.R.C.P.& S.Ed., L.R.F.P.S., late of Gosforth, Newcastle-upon-Tyne.

**Harvey.**—On May 23, 1951, at Bermuda, Eugenius Harvey, M.R.C.S., L.R.C.P.

**Martin.**—On May 18, 1951, at 12, Croxteth Road, Liverpool, John Graham Martin, M.D., Colonel, A.M.S., retired.

**Pringle.**—On May 24, 1951, at Hong Kong, Leonard Duncan Pringle, M.R.C.S., L.R.C.P., formerly of Finchley, London, N.

**Rankin.**—On May 19, 1951, at 58, Cleveden Drive, Glasgow, Frederick Powlett Rankin, O.B.E., M.B., Ch.B., Lieutenant-Colonel, R.A.M.C., retired.

**Sullivan.**—On May 23, 1951, at South Kirkby, Yorks, Fleetwood William Porter Sullivan, M.D.

**Upcott.**—On May 24, 1951, at China Garth, Thornton-le-Dale, Yorks, Harold Upcott, F.R.C.S., aged 71.

# Any Questions?

### Bacillary Dysentery Carriers

**Q.**—*I have lately come across a few cases of Flexner and Sonne dysentery which clear up clinically on treatment but give positive stool results for many weeks afterwards in spite of repeated courses of sulphonamides. What drugs are likely to be most effective in the treatment of these "chronic excreters"? Is there a "carrier" condition in bacillary dysentery in any way comparable to that in typhoid?*

**A.**—Persistent excreters of *Shigella flexneri* are rare. Organisms of this group live and multiply in the superficial layers of the mucous membrane, and such persistent excreters are therefore suffering from mild chronic infections. *S. sonnei*, on the other hand, is more closely related to the non-pathogenic coliform organisms and can live and multiply in the contents of the bowel. This organism frequently persists for long periods after symptoms have disappeared, and subjects infected in this way can be regarded as true carriers. The most favoured sulphonamides for the treatment of persistent excreters are the slowly absorbed compounds sulphaguanidine, succinylsulphathiazole, and phthalylsulphathiazole, but these are frequently ineffective. Good results have been achieved in some cases with the newer antibiotics, particularly chloramphenicol. This is given orally in a dosage of 250 mg. four-hourly for 6 to 10 days, and is claimed to produce a rapid clearance.

### Sore Tongue

**Q.**—*For the past five years a boy of 18 has complained of pain in his tongue brought on by eating acid foods or highly spiced dishes such as curry and haggis. This is followed by soreness for about half an hour. Examination shows a tongue deeply furrowed transversely which is a little redder than normal, with fairly prominent papillae at the tip. There is no coating on it, and from every other point of view he seems perfectly fit. Urine examination, Wassermann and Kahn tests, and haematological examination are negative. A swab from the tongue produced on culture Neisseria pharyngis with a few colonies of Streptococcus viridans and haemolytic streptococci. There can be little doubt that he has a congenital furrowed tongue, with, I suppose, the possibility of a chronic glossitis. I can find little about these symptoms of sore tongue in the books. What line of treatment would you advise?*

**A.**—The aetiology and treatment of a sore and painful tongue are difficult and often complex problems. The commonest association is with achlorhydria, so that sore tongue is a feature of pernicious anaemia and hypochromic microcytic anaemia, and it may also occur in non-anaemic achlorhydric patients. In these cases the condition nearly always clears up on a hydrochloric acid and pepsin mixture taken in plenty of water through a glass tube after meals. Where anaemia is present then the appropriate therapy should be given. There is, however, a group of cases associated with hyperacidity, and often there appears to be a multiple vitamin deficiency of mainly the vitamin-B complex. Some of these cases will respond to an alkaline mixture (for the hyperacidity) and a high vitamin intake; one of the vitamin-B-complex mixtures may be prescribed. Particularly do these cases seem to require nicotinic acid, aneurin, and folic acid, with sometimes the addition of vitamin A. Again, any mild degree of hypochromic anaemia should be treated appropriately.

There is a further group of cases seen in young women which takes the form of a cyclical mucosal ulceration of the tongue and mouth which occasionally also involves the vaginal membrane. It often comes on before the menstrual

period, and it may clear up during or after, recurring again with the next period. This is a very intractable condition to treat, but some relief has been reported from the use of testosterone, and sometimes from oestrogen therapy, with the addition of the vitamin and anti-anaemic therapy as described above.

In the case of the boy concerned in this question he should have first a test meal.

### Exercises for a Protuberant Belly

**Q.**—*A patient, aged 26, has just spent three months in bed, and she now has a very prominent abdomen—partly due to excess subcutaneous fat and partly due to very relaxed abdominal muscles. She has the appearance of being about five months pregnant, although she is really quite thin. Can you suggest some good exercises for her, and also some way of reducing the abdominal fat?*

**A.**—The essential feature in treating this patient is to improve her muscle tone; in such cases the subcutaneous fat is almost always a very minor factor, and if the abdominal wall returns to normal tone the fat will hardly be noticed. There is no local method of reducing the fat.

It is important to stress that the patient should try to hold in her abdominal muscles tightly all the time, but especially when standing; after a while the muscles will remain in better tone habitually. In addition to this, simple exercises should be carried out to improve muscle tone; but unless a full course is carried out under the supervision of a physiotherapist it is always wise to keep these exercises as few as possible, otherwise patients tend to neglect them. It is therefore suggested that the patient should practise contracting the recti abdominis some 30 times morning and evening while lying down; she can also contract them at intervals during the day when she is either sitting or standing. The two following exercises should also be performed 12 times every morning and evening: the patient lies on her back and slowly raises both legs together and slowly lowers them again; then with the toes fixed under a firm rail she raises her body to a sitting position without using her hands.

### Hexamine

**Q.**—*Hexamine was the main urinary antiseptic a few years back. Why is it no longer included in the "British Pharmacopoeia"?*

**A.**—Hexamine is no longer included in the *British Pharmacopoeia* because its value as a urinary antiseptic has always been small and it does not compare in efficiency with ammonium or calcium mandelate or with the sulphonamides, such as sulphathiazole, or with the antibiotics, such as streptomycin. Hexamine has therefore been entirely replaced by these newer agents, particularly the sulphonamides.

### Barrier Creams and Eczema

**Q.**—*There are a number of barrier creams on the market intended primarily to keep clean the hands of those employed in dirty types of work. Two creams in common use protect the skin against liquids, waterproofing it, as well as against solid dirt. Would such creams be useful in the treatment of the types of eczema which are exacerbated by either water-soluble substances or by household dirt and dust?*

**A.**—Barrier creams are meant to be applied to normal and not damaged skin. They leave a more or less occlusive film on the epidermis to protect against external irritants. This must usually be harmful if there is an underlying inflammatory lesion.

There are numerous types of barrier creams. Many containing soaps are alkaline, and so are somewhat irritant. Most contain fats and higher fatty alcohols and various inert emulsifying bases. Upon occasion patients show sensitivity to some of the ingredients. As a rule, therefore, barrier creams are not suited to the treatment of eczema, for which they are not intended. Nevertheless some patients with mild chronic dry eczematization do find these creams quite helpful.

### Allergy and Immunization

**Q.**—*A female infant, aged 11½ months, was recently admitted to a children's hospital as an emergency. The history was that after taking a little fish she developed a rash, and parts of the body swelled, especially the eyelids, which were completely closed. She was discharged cured in three days, with a diagnosis of "angioneurotic oedema due to fish-poisoning." The family history is that the child's mother suffered in a similar manner at the same age after taking fish, and since then at intervals has suffered from attacks of asthma. There is also a more distant relative who suffers from asthma. The father has no history of allergic disorder.*

*The mother is anxious that the child should be immunized against most of the infectious fevers. Is this desirable or dangerous?*

**A.**—Immunization is desirable and without risk. For diphtheria, the alum-precipitated toxoid should be used and not the toxoid-antitoxin. Immunization to tetanus might also be considered later, as it would avoid the necessity of antitetanic serum with its risks in an allergic subject in the event of a skin laceration in later years.

### Paget's Disease of Bone

**Q.**—*Is there any treatment at present for osteitis deformans, particularly where it is giving rise to pain in the muscles of the calves?*

**A.**—Osteitis deformans (Paget's disease) causes no symptoms in most cases. In a few there is an aching pain in the region of the affected bone. When other symptoms are experienced the possibility of some complication, or of associated diseases, must be borne in mind. Important complications are fracture and sarcoma; and commonly associated diseases are osteoarthritis and occlusive vascular disease. Before treatment is advised for Paget's disease these possibilities should be eliminated by careful clinical investigations (including an assessment of the peripheral circulation) and adequate radiographic examination.

Treatment of Paget's disease is disappointing. The cause of the condition being unknown, most methods of treatment are empirical. Agents that have been tried include calcium, phosphates, *x*-ray therapy, and longitudinal osteotomy. But it cannot be said that any of them can be relied upon to afford important relief.

### Methaemoglobinaemia in Industry

**Q.**—*In the "Chemist and Druggist" (December 9, 1950, p. 661) it is stated that para-aminopropiophenone produces methaemoglobinaemia in mice. Is there any evidence that this substance can produce methaemoglobinaemia in humans? Also, is there any evidence that para-nitroacetaminohydroxypropiophenone can produce methaemoglobinaemia? Men in a certain industry are exposed to the latter both by skin contact and also by inhalation.*

**A.**—There is no reference in the literature to methaemoglobinaemia in human beings due to absorption of *para*-aminonitrophenone or to *para*-nitroacetaminohydroxypropiophenone. The chemical structure suggests that both substances could cause the conversion of haemoglobin to methaemoglobin, but the prediction of toxic effects from a study of chemical structure cannot be made with certainty.

# FESTIVAL SCIENTIFIC MEETINGS

There has been a considerable demand for tickets for the Symposia arranged throughout June at the Royal Society of Medicine. The following meetings are now full, and members are advised to apply *as early as possible* for the remaining sessions:

| *Date and Time* | *Subject* |
|---|---|
| Monday, June 4, 2 p.m. .. | The Peripheral Nervous System |
| Thursday, June 7, 2.15 p.m. .. | Antibiotics |
| Friday, June 8, 4 p.m. .. | Vascular System (Clinical) |
| Thursday, June 14, 2 p.m. .. | Central Nervous System |
| Monday, June 18, 2.15 p.m. .. | Endocrinology (Clinical) |
| Wednesday, June 20, 10 a.m. | Peptic Ulcer |
| Monday, June 25, 10 a.m. .. | Cortisone and A.C.T.H. |

## PROGRAMME OF SYMPOSIA

### *Monday, June 4*

2 p.m.—THE PERIPHERAL NERVOUS SYSTEM. *Chairman*, Sir HENRY DALE, O.M., G.B.E., M.D., F.R.S. Professor G. L. BROWN, Transmission in Sympathetic Ganglia; Dr. B. KATZ, The Response of the Motor End-plate to a Nerve Impulse; Dr. W. S. FELDBERG, Mechanisms of Neuromuscular Block; Professor J. H. BURN, The Relation of *Nor*adrenaline to Adrenaline; Professor J. Z. YOUNG, Determination of the Size of Nerve Fibres; Mr. H. J. SEDDON, Recent Advances in the Repair of Injured Nerves; Dr. D. C. SINCLAIR, The Anatomy of Pain Sensibility.

### *Wednesday, June 6*

10.30 a.m.—OTORHINOLARYNGOLOGY. *Chairman*, W. M. MOLLISON, C.B.E., M.Ch. *Recent Advances in Otology.* (1) Hearing-aids: Dr. T. S. LITTLER, The Development of the Medresco Aid; Mr. J. OTTY, Clinical Experiences with the Medresco Aid; Mr. P. G. GRAY, The Medresco Aid in Use—Patients' Experiences. (2) Hearing Tests: Mr. C. S. HALLPIKE, The Clinical Tests of Cochlear Function, Recent Developments of Theory and Practice. (3) The Surgery of the Labyrinth, Mr. TERENCE CAWTHORNE.

2.30 p.m.—*Malignant Disease of the Upper Respiratory Passages.* Mr. F. C. W. CAPPS, Malignant Disease of the Nose and Paranasal Sinuses; Professor F. C. ORMEROD, Malignant Disease of the Nasopharynx and Oropharynx; Mr. V. E. NEGUS, Malignant Disease of the Pharyngolarynx and Larynx; Dr. H. A. LUCAS, The Pathology of Malignant Disease of the Upper Respiratory Passages; Dr. GWEN HILTON and Mr. T. M. PROSSOR, The Radiotherapy of Malignant Disease of the Upper Respiratory Passages.

### *Thursday, June 7*

2.15 p.m.—ANTIBIOTICS. *Chairman*, Professor Sir ALEXANDER FLEMING, F.R.C.S., F.R.S. Professor Sir HOWARD FLOREY, Some Observations on the Antimicrobial Products of Fungi and Bacteria; Dr. E. P. ABRAHAM, Some Chemical Aspects of Antibiotics from Fungi and Bacteria; Dr. E. LESTER SMITH, The Production of Antibiotics; Professor L. P. GARROD, Acquired Resistance to Antibiotics; Professor CLIFFORD WILSON, Clinical Evaluation of Antibiotic Therapy; Dr. G. L. M. MCELLIGOTT, Antibiotics in Venereal Disease; Professor ROBERT CRUICKSHANK, Antibiotics in Infectious Disease.

### *Friday, June 8*

4 p.m.—THE VASCULAR SYSTEM (Clinical). *Chairman*, Sir JOHN PARKINSON, M.D. Sir JAMES LEARMONTH, Surgery of the Arteries; Professor J. MCMICHAEL, Cardiac Failure; Dr. R. T. GRANT, Wound Shock; Professor G. W. PICKERING, Essential Hypertension.

### *Monday, June 11*

2.30 p.m.—OPHTHALMOLOGY. *Chairman*, A. W. S. SICHEL, M.D., D.O. (President-Elect, B.M.A., 1951–2). Dr. L. C. THOMSON, Colour Vision; Dr. W. A. H. RUSHTON, Electrophysiology of the Retina; Mr. B. W. RYCROFT, Corneal Grafts (with film); Mr. A. G. CROSS, Contact Lenses; Professor ARNOLD SORSBY, Genetics in Ophthalmology.

### *Tuesday, June 12*

10.30 a.m.—PLASTIC SURGERY. *Chairman*, Sir GORDON GORDON-TAYLOR, K.B.E., M.S. Sir HAROLD GILLIES, General Review; Sir WILLIAM KELSEY FRY, The External Ear; Mr. RAINSFORD MOWLEM, Report on the Development of the Cancellous Chip Bone Graft.

2 p.m.—PLASTIC SURGERY (*cont.*). *Chairman*, Professor Sir JAMES PATERSON ROSS, K.C.V.O., M.S. Professor T. POMFRET KILNER, Congenital Clefts of the Lip and Palate; Sir ARCHIBALD MCINDOE, Reconstruction of the Burned Face; Mr. RAINSFORD MOWLEM and Mr. L. W. PLEWES, Orthoplastics in Industry.

### *Thursday, June 14*

2 p.m.—THE CENTRAL NERVOUS SYSTEM. *Chairman*, W. RUSSELL BRAIN, D.M., P.R.C.P. Professor W. E. LE GROS CLARK, The Contribution of Anatomy to Problems of Sensory Discrimination; Professor E. G. T. LIDDELL, Stimulation of the Motor Cortex in Monkeys; Dr. F. M. R. WALSHE, Some Principles Governing the Interpretation of Experimental Studies of Cortical Function, with Special Reference to the Organization of Movements; Dr. GREY WALTER, The Physiology of Adaptive Behaviour.

### *Friday, June 15*

4.30 p.m.—ANAESTHETICS. *Chairman*, I. W. MAGILL, C.V.O., M.B., D.A. Professor E. A. PASK, Research; Dr. JOHN GILLIES and Dr. G. E. H. ENDERBY, Controlled Circulation; Dr. CECIL GRAY, Relaxants; Dr. W. W. MUSHIN, Supplementary Agents; Dr. M. D. NOSWORTHY, Thoracic Surgery; Dr. A. I. PARRY BROWN, Cardiac Surgery.

### *Monday, June 18*

10 a.m.—POLIOMYELITIS. *Chairman*, F. M. R. WALSHE, O.B.E., M.D., F.R.S. Dr. F. O. MACCALLUM, Virus Infection; Dr. D. MCALPINE, The Early Symptomatology of Virus Infection; Dr. W. H. KELLEHER, The Management of the Early Stage of Poliomyelitis; Mr. H. J. SEDDON, Poliomyelitis, the Convalescent Stage; Dr. A. H. GALE, Poliomyelitis as an Epidemic Disease in England and Wales.

2.15 p.m.—ENDOCRINOLOGY (Clinical). *Chairman*, R. D. LAWRENCE, M.D. Dr. HAROLD GARDINER-HILL, Obesity and Carbohydrate Metabolism; Dr. R. D. LAWRENCE, Two Types of Diabetes—With and Without Blood-insulin; Dr. P. M. F. BISHOP, The Oestrogens: Their Clinical Use; Dr. LEONARD SIMPSON, Pituitary-Adrenal Hyperfunction.

### *Tuesday, June 19*

10 a.m.—THE DECLINE OF INFANT MORTALITY. *Chairman*, Sir ALLEN DALEY, M.D., D.P.H. Sir JAMES SPENCE, Maternal Skill and Other Factors Responsible for the Decline of Infant Mortality; Professor T. MCKEOWN, Congenital Malformations; Professor T. N. A. JEFFCOATE, From the Angle of the Obstetrician; Dr. H. K. WALLER, Breast Feeding.

5 p.m.—BURNS. *Chairman*, LEONARD COLEBROOK, M.B., F.R.S. Dr. J. P. BULL, The Problem of Fluid Replacement; Dr. E. J. L. LOWBURY, The Control of Infection; Mr. DOUGLAS JACKSON, Physical Signs which Indicate the Need for Grafting; Dr. P. DALLAS ROSS, Early Skin-grafting; Mr. RAINSFORD MOWLEM, The Use of Homografts for Extensive Burns; Mr. A. B. WALLACE, The Exposure Method of Treating Burns.

*Wednesday, June 20*

10 a.m.—PEPTIC ULCER. *Chairman*, Professor Sir HENRY COHEN, M.D., F.R.C.P. Mr. NORMAN TANNER, The Role of Surgery in the Treatment of Peptic Ulcer; Dr. F. AVERY JONES, The Physician's Viewpoint; Dr. S. COCHRANE SHANKS, *X*-ray Diagnosis of Peptic Ulcer; Dr. HENRY WILSON, Psychological Factors.

2.15 p.m.—EXPERIMENTAL ENDOCRINOLOGY. *Chairman*, A. S. PARKES, D.Sc., F.R.S. Professor E. C. DODDS, Synthetic Oestrogens; Professor F. G. YOUNG, The Endocrine Approach to the Problem of Diabetes; Dr. G. W. HARRIS, The Hypothalamo-Hypophysial Link in the Stress Syndrome; Professor E. B. VERNEY, The Excretion of Water and its Physiological Regulation; Dr. S. J. FOLLEY, Endocrine Factors in Lactation.

*Thursday, June 21*

10 a.m.—NUTRITION AND THE B VITAMINS. *Chairman*, Lord HORDER, G.C.V.O., M.D. Dr. R. A. PETERS, The Clinical Implications of Research on Vitamin $B_1$; Dr. LESTER SMITH and Dr. BODLEY SCOTT, Treatment of the Macrocytic Anaemias; Professor B. S. PLATT, B Deficiencies in the Tropics; Dr. L. J. HARRIS, Nicotinamide and Pellagra.

2 p.m.—NEUROSURGERY. *Chairman*, Professor Sir HUGH CAIRNS, K.B.E., F.R.C.S. Professor N. M. DOTT and Mr. G. L. ALEXANDER, Intracranial Aneurysmal Malformations; Professor Sir GEOFFREY JEFFERSON, The Frontal Lobe; Professor Sir HUGH CAIRNS, Head Injuries; Mr. J. B. PENNYBACKER, Abscess of the Brain; Mr. HARVEY JACKSON, Tumours of the Orbit; Dr. L. GUTTMANN, The Care of the Paraplegic Patient.

*Friday, June 22*

10 a.m.—THE PROBLEMS OF CARDIOVASCULAR DISEASE IN AN AGEING POPULATION. *Chairman*, J. H. SHELDON, M.D., F.R.C.P. Professor A. M. BOYD, The Diagnosis and Management of Circulatory Deficiency in the Lower Extremity due to Degenerative Arterial Disease; Dr. WILLIAM EVANS, Cardiac Pain; Dr. T. ROWLAND HILL, Neurological Aspects; Dr. D. D. REID, Incidence.

2.15 p.m.—ORTHOPAEDICS. Chairman, S. L. HIGGS, F.R.C.S., President, British Orthopaedic Association. Sir HARRY PLATT, Unusual Malignant Tumours of Bone; Sir GORDON GORDON-TAYLOR, The Surgery of Malignant Disease in the Vicinity of the Hip-joint; Sir THOMAS FAIRBANK, Some General Affections of the Skeleton; Mr. BRYAN MCFARLAND, Developmental Defects of Long Bones.

*Monday, June 25*

10 a.m.—CORTISONE AND A.C.T.H. *Chairman*, Professor G. R. CAMERON, F.R.C.P., F.R.S. Dr. G. W. HARRIS, The Clinical Implications of Recent Research Work on the Pituitary and Adrenal Glands; Dr. W. S. C. COPEMAN and Dr. OSWALD SAVAGE, The Rheumatic Diseases; Dr. D. LONG, Cortisone and Allergy; Dr. F. T. G. PRUNTY, Effects of A.C.T.H. and Cortisone in Acute Disseminated Lupus Erythematosus and Dermatomyositis; Professor HENRY MOORE, Experiences with Cortisone in Dublin, with Special Reference to Toxaemia of Pregnancy.

4 p.m.—THE PHYSIOLOGY OF THE VASCULAR SYSTEM. *Chairman*, Lord HORDER, G.C.V.O., M.D. Professor K. J. FRANKLIN, The Change-over in the Circulation During and Shortly After Birth; Professor I. DE BURGH DALY, The Pulmonary Circulation; Dr. D. A. MCDONALD and Dr. J. M. POTTER, Some Remarks on Circulatory Rheology, with the Following Films: (*a*) Blood Streams in the Basilar Artery, (*b*) Velocity of the Blood Flow in the Basilar Artery; Professor J. TRUETA, The Renal Circulation; Professor H. BARCROFT, The Action of Adrenaline and *Nor*adrenaline on the Human Circulation.

*Tuesday, June 26*

10 a.m.—THE DIAGNOSIS AND MANAGEMENT OF EARLY MENTAL DISORDERS. *Chairman*, DESMOND CURRAN, F.R.C.P., D.P.M. Dr. NOEL HARRIS, The Psychiatrist's Viewpoint; Dr. J. C. SAWLE THOMAS, From the Angle of the Regional Psychiatrist; Dr. THOMAS BEATON, The Mental Hospital in Relation to the General Public; Dr. KENNETH CAMERON, The Child Psychiatrist's Viewpoint.

4.30 p.m.—TROPICAL MEDICINE. *Chairman*, Sir PHILIP MANSON-BAHR, C.M.G., F.R.C.P. Professor H. E. SHORTT, Protozoology and World Economic Problems; Professor B. G. MAEGRAITH, Physiological Approach to Tropical Medicine; Sir NEIL HAMILTON FAIRLEY, Chemotherapy in the Control and Treatment of Malaria.

*Wednesday, June 27*

10 a.m.—REACTIONS IN GENERAL PRACTICE TO SCIENTIFIC ADVANCES. *Chairman*, G. F. ABERCROMBIE, M.D. Dr. LAWRENCE DULAKE, Reactions in General Practice to Scientific Advances; Mr. JOHN EVERIDGE, Personal Impressions of Some Advances in Urology of Significance to the General Practitioner; Dr. H. GUY DAIN, Changes in General Practice During the Past Twenty-five Years as Seen by a General Practitioner; Dr. GEOFFREY EVANS, Changes in General Practice During the Past Twenty-five Years as Seen by a Consultant Physician; Dr. WILFRED OAKLEY, Diabetes and Modern Therapy.

4.30 p.m.—EPIDEMIOLOGY. *Chairman*, W. H. BRADLEY, D.M. Dr. C. H. ANDREWES, Influenza and the Common Cold; Dr. W. N. PICKLES, Virus Diseases in General Practice.

*Thursday, June 28*

10 a.m.—CARCINOMA OF THE LUNG. *Chairman*, T. HOLMES SELLORS, M.Ch. Introduction by Mr. R. C. BROCK. Professor D. W. SMITHERS and Mr. C. PRICE THOMAS, The Place of Radiotherapy in the Treatment of Bronchial Carcinoma; Dr. N. LLOYD RUSBY, From the Angle of the Physician; Dr. W. R. S. DOLL, The Relationship Between Smoking and Bronchial Carcinoma.

2.15 p.m.—THORACIC SURGERY. *Chairman*, N. R. BARRETT, M.Ch. Mr. P. R. ALLISON, The Anatomy and Physiology of the Oesophagogastric Junction in Relation to Hiatal Hernia and Oesophageal Ulceration; Mr. C. PRICE THOMAS, The Surgery of Adenoma of the Bronchus; Mr. R. C. BROCK, Intracardiac Surgery.

*Monday, July 9*

4 p.m.—ODONTOLOGY. *Chairman*, Sir WILLIAM KELSEY FRY, C.B.E., M.D.S., F.D.S. *The Significance of Dental Sepsis to the Physician, the Ear, Nose, and Throat Surgeon, the Ophthalmologist, and the Dermatologist.* The Physician, Dr. A. H. DOUTHWAITE; The Ear, Nose, and Throat Surgeon, Mr. C. GILL-CAREY; The Ophthalmologist, Mr. J. H. DOGGART; The Dermatologist, Dr. W. J. O'DONOVAN. The subsequent discussion will be opened by Dr. WILFRED FISH and Professor MARTIN RUSHTON.

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